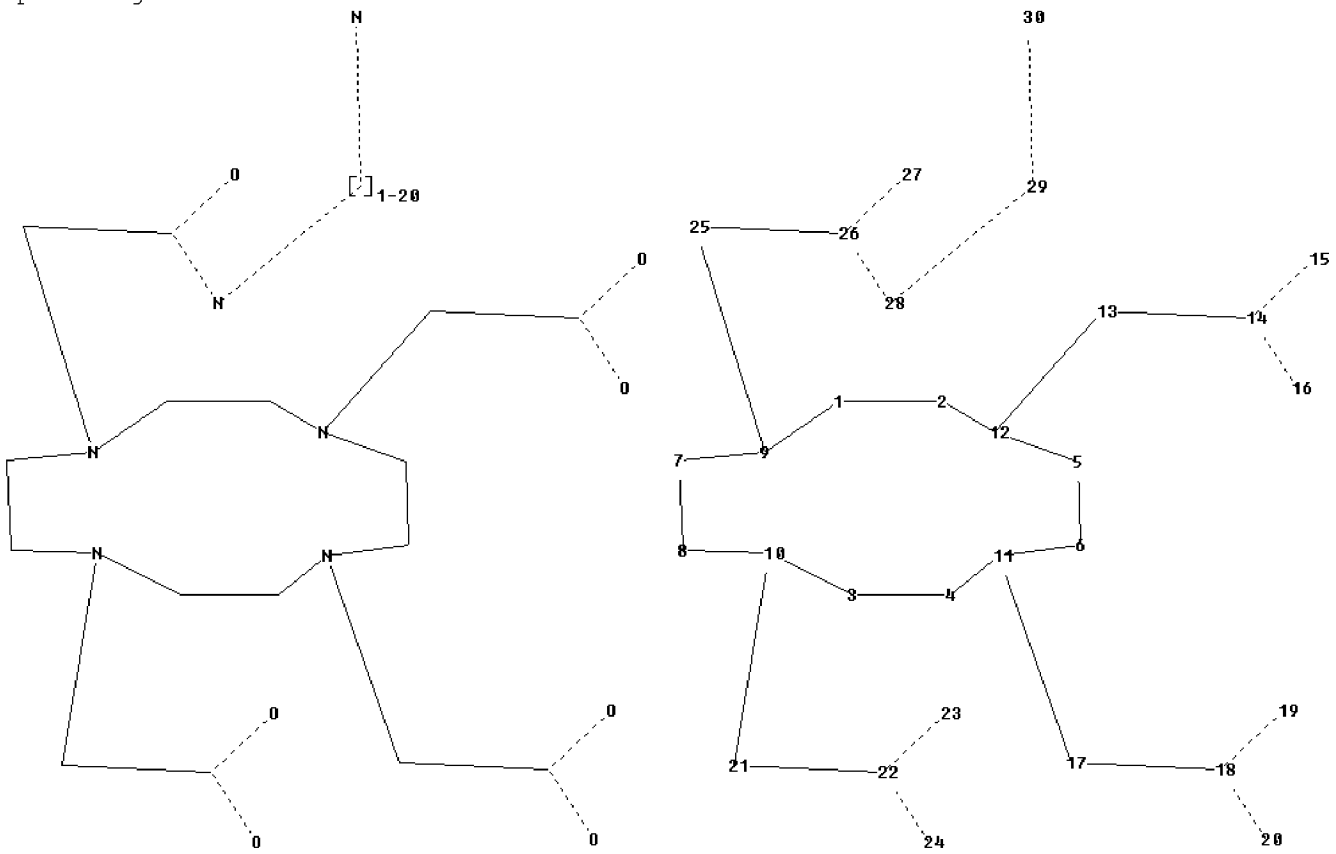
```
=> file registry
FILE 'REGISTRY' ENTERED AT 10:20:59 ON 21 FEB 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   20 FEB 2008  HIGHEST RN 1004854-20-9
DICTIONARY FILE UPDATES:  20 FEB 2008  HIGHEST RN 1004854-20-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> file zcaplus
FILE 'ZCAPLUS' ENTERED AT 10:21:01 ON 21 FEB 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS is
strictly prohibited.

FILE COVERS 1907 - 21 Feb 2008  VOL 148 ISS 8
FILE LAST UPDATED: 20 Feb 2008  (20080220/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

=> d stat que L73
L68          96 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  GARLICH J?/AU
L69          49 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  SUHR R?/AU
L70         710 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  PATTERSON M?/AU
L71           5 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L68 AND (L69 OR L70)
L72           4 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L69 AND L70
L73           5 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  (L71 OR L72)
```

```
=> d stat que L74
L25             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation:
Uploading L25.str
```




```
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12
ring/chain nodes :
13  14  15  16  17  18  19  20  21  22  23  24  25  26  27  28  29  30
ring/chain bonds :
9-25  10-21  11-17  12-13  13-14  14-16  14-15  17-18  18-20  18-19  21-22  22-24
22-23  25-26  26-28  26-27  28-29  29-30
ring bonds :
1-2  1-9  2-12  3-4  3-10  4-11  5-6  5-12  6-11  7-8  7-9  8-10
exact/norm bonds :
1-2  1-9  2-12  3-4  3-10  4-11  5-6  5-12  6-11  7-8  7-9  8-10  9-25  10-21  11-
17
12-13  13-14  14-16  14-15  17-18  18-20  18-19  21-22  22-24  22-23  25-26  26-28
26-27  28-29
29-30


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS
19:CLASS  20:CLASS  21:CLASS
```

```
22:CLASS  23:CLASS  24:CLASS  25:CLASS  26:CLASS  27:CLASS  28:CLASS  29:CLASS
30:CLASS



L29        2020 SEA FILE=REGISTRY SSS FUL L25
L68          96 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  GARLICH J?/AU
L69          49 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  SUHR R?/AU
L70         710 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  PATTERSON M?/AU
L74           1 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L29 AND (L68 OR L69 OR L70)


=> s L73-L74
L75           5 (L73 OR L74)

=> file medline embase biosis
FILE 'MEDLINE' ENTERED AT 10:21:26 ON 21 FEB 2008

FILE 'EMBASE' ENTERED AT 10:21:26 ON 21 FEB 2008
Copyright (c) 2008 Elsevier B.V. All rights reserved.

FILE 'BIOSIS' ENTERED AT 10:21:26 ON 21 FEB 2008
Copyright (c) 2008 The Thomson Corporation

=> s L73
L76           1 L73

=> file wpix
FILE 'WPIX' ENTERED AT 10:21:40 ON 21 FEB 2008
COPYRIGHT (C) 2008 THE THOMSON CORPORATION

FILE LAST UPDATED:                        20 FEB 2008   <20080220/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE:     200812       <200812/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> IPC Reform backfile reclassification has been loaded to the end of
    November 2007. No update date (UP) has been created for the
    reclassified documents, but they can be identified by
    20060101/UPIC and 20061231/UPIC, 20070601/UPIC, 20071001/UPIC and
    20071130/UPIC. <<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:
http://www.stn-international.com/archive/presentations/DWPIAnaVist2_0710.pdf

>>> XML document distribution format now available - See HELP XMLDOC <<<

>>> ECLA Codes and Current US National Classifications have been added -
    see NEWS and HELP CHANGE <<<

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<
```

```
>>> Updated PDF files in the following links:
    http://www.stn-international.de/stndatabases/details/ico_0801.zip
    http://www.stn-international.de/stndatabases/details/epc_0801.zip <<<
'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> s L73
            34 GARLICH J?/AU
            32 SUHR R?/AU
           178 PATTERSON M?/AU
            32 SUHR R?/AU
           178 PATTERSON M?/AU
L77          2 (L71 OR L72)

=> file stnguide
FILE 'STNGUIDE' ENTERED AT 10:21:48 ON 21 FEB 2008
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 15, 2008 (20080215/UP).

=> dup rem L75 L76 L77
FILE 'ZCAPLUS' ENTERED AT 10:22:04 ON 21 FEB 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 10:22:04 ON 21 FEB 2008
Copyright (c) 2008 Elsevier B.V. All rights reserved.

FILE 'WPIX' ENTERED AT 10:22:04 ON 21 FEB 2008
COPYRIGHT (C) 2008 THE THOMSON CORPORATION
PROCESSING COMPLETED FOR L75
PROCESSING COMPLETED FOR L76
PROCESSING COMPLETED FOR L77
L78           5 DUP REM L75 L76 L77 (3 DUPLICATES REMOVED)
                ANSWERS '1-5' FROM FILE ZCAPLUS

=> d ibib abs hitind hitstr L78 1-5

L78  ANSWER 1 OF 5  ZCAPLUS  COPYRIGHT 2008 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2005:324033  ZCAPLUS  Full-text
DOCUMENT NUMBER:          142:379479
TITLE:                    Chelate based scaffolds in tumor targeting
INVENTOR(S):              Garlich, Joseph R.; Suhr, Robert G.; Patterson, Mary
PATENT ASSIGNEE(S):       Semafore Pharmaceuticals Inc., USA
SOURCE:                   PCT Int. Appl., 47 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
     WO 2005032599        A1    20050414    WO 2004-US32289        20040930
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
```

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1684809 A1 20060802 EP 2004-789423 20040930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

US 2007104645 A1 20070510 US 2006-573938 20060725

PRIORITY APPLN. INFO.: US 2003-507427P P 20030930
WO 2004-US32289 W 20040930

AB This invention relates to novel complexes that can be used to target tumor cells. The complexes include a ligand including a tetraazacyclododecane macrocycle ring core that can bind metal ions including radioactive lanthanide ions. The complexes can mimic αvβ3 integrin receptor antagonists and deliver the complexed radioactive metals to the tumor cells. For example, 24.4 mM of cyclen reacted with 24.4 mM of tert-Bu bromoacetate to give 5.72 g 1,4-DO2A bis-tert-Bu ester (82% of theory) as clear viscous oil. The oil was dissolved in MeOH, allowed to crystallize, the solid obtained was filtered, washed with water and then dried to give 4.3964 g of white solid.

IC ICM A61K051-00

CC 63-8 (Pharmaceuticals)
Section cross-reference(s): 1, 8, 24

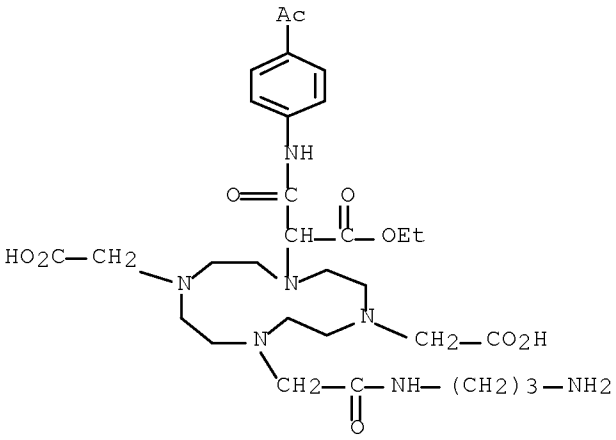
IT 849610-60-2P 849610-61-3P 849610-62-4P 849610-63-5P
849610-64-6P 849610-65-7P 849610-66-8P
849610-67-9P 849610-68-0P 849610-69-1P
849610-70-4P 849610-71-5P 849610-72-6P
849610-73-7P 849610-74-8P 849610-75-9P
849610-76-0P 849610-77-1P 849610-78-2P
849610-79-3P 849610-80-6P 849610-81-7P
849610-82-8P 849610-83-9P 849610-84-0P
849610-85-1P 849610-86-2P 849610-87-3P
849610-88-4P 849610-89-5P 849610-90-8P
849610-91-9P 849610-92-0P 849610-93-1P
849610-94-2P 849610-95-3P 849610-96-4P
849610-97-5P 849610-98-6P 849610-99-7P 849611-00-3P
849680-88-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chelate-based scaffolds for tumor targeting)

IT 849610-60-2P 849610-65-7P 849610-66-8P
849610-67-9P 849610-68-0P 849610-69-1P
849610-70-4P 849610-71-5P 849610-72-6P
849610-73-7P 849610-74-8P 849610-75-9P
849610-76-0P 849610-77-1P 849610-78-2P
849610-79-3P 849610-80-6P 849610-81-7P
849610-82-8P 849610-83-9P 849610-84-0P
849610-85-1P 849610-86-2P 849610-87-3P
849610-88-4P 849610-89-5P 849610-90-8P
849610-91-9P 849610-92-0P 849610-93-1P
849610-94-2P 849610-95-3P 849610-96-4P
849680-88-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chelate-based scaffolds for tumor targeting)

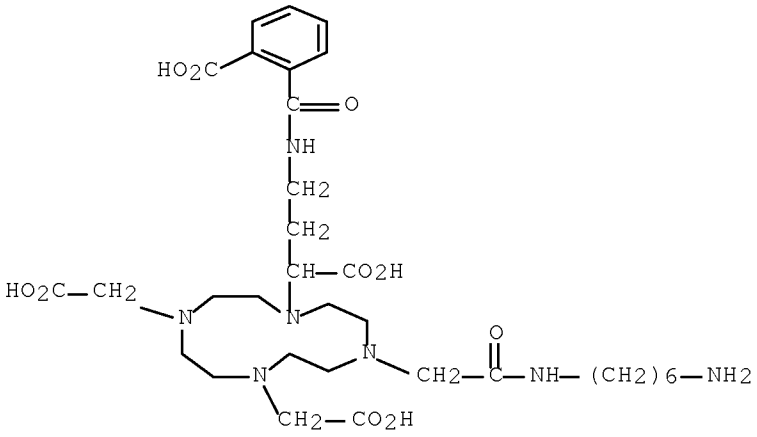
RN 849610-60-2 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, α4-[[(4-acetylphenyl)amino]carbonyl]-10-[2-[(3-aminopropyl)amino]-2-oxoethyl]-,

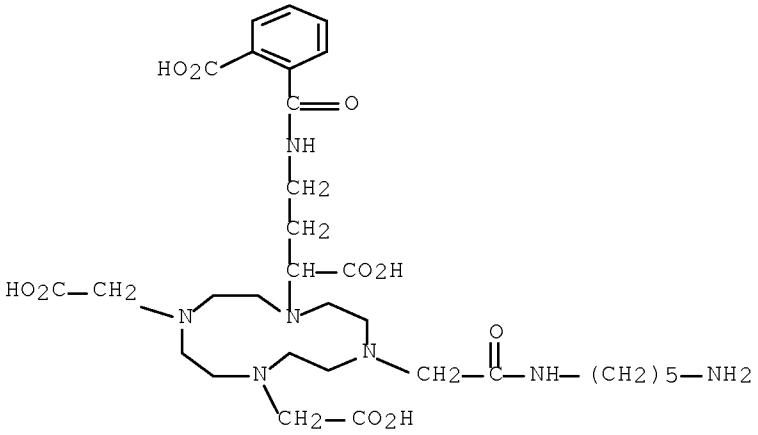
α4-ethyl ester (9CI) (CA INDEX NAME)



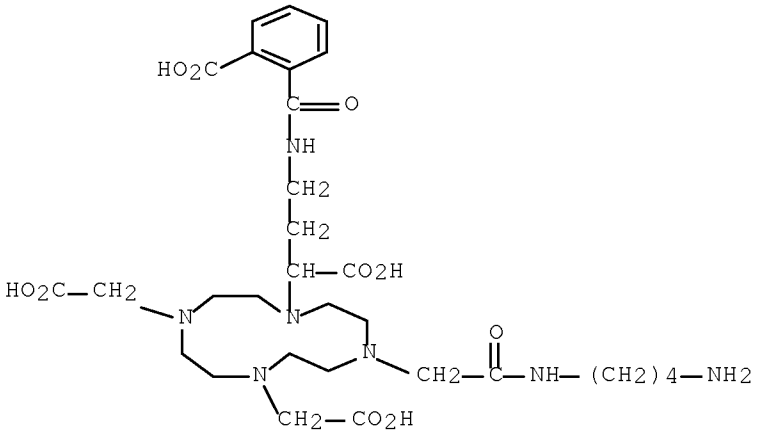
RN 849610-65-7 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-aminohexyl)amino]-2-oxoethyl]-α-[2-[(2-carboxybenzoyl)amino]ethyl]- (9CI) (CA INDEX NAME)



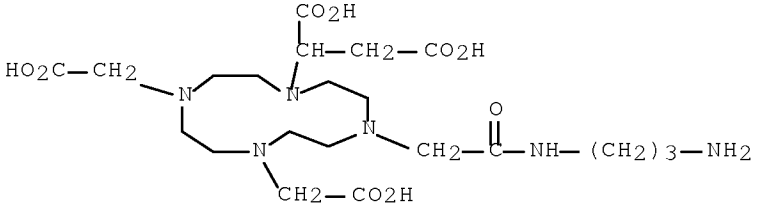
RN 849610-66-8 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(5-aminopentyl)amino]-2-oxoethyl]-α-[2-[(2-carboxybenzoyl)amino]ethyl]- (9CI) (CA INDEX NAME)



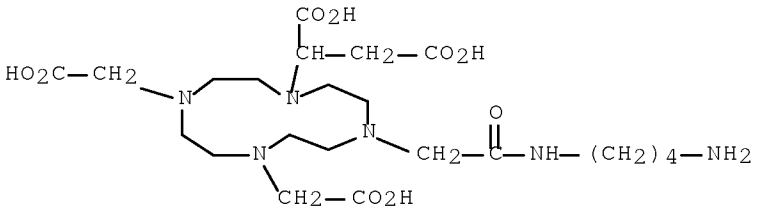
RN 849610-67-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(4-aminobutyl)amino]-2-oxoethyl]-α-[2-[(2-carboxybenzoyl)amino]ethyl]- (CA INDEX NAME)



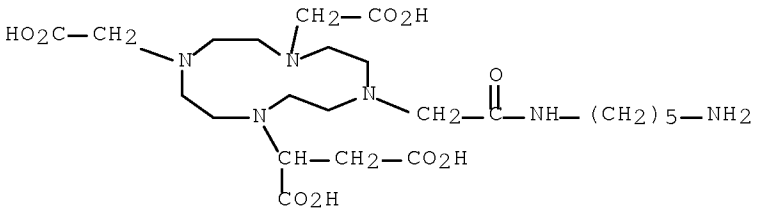
RN 849610-68-0 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(3-aminopropyl)amino]-2-oxoethyl]-α-(carboxymethyl)- (9CI) (CA INDEX NAME)



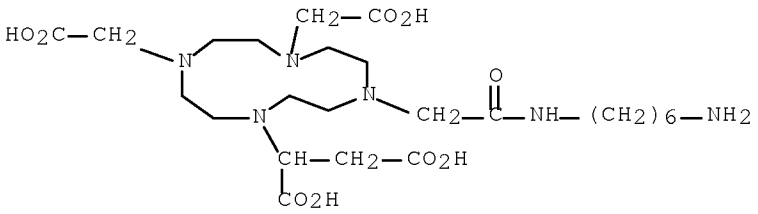
RN 849610-69-1 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(4-aminobutyl)amino]-2-oxoethyl]-α-(carboxymethyl)- (9CI) (CA INDEX NAME)



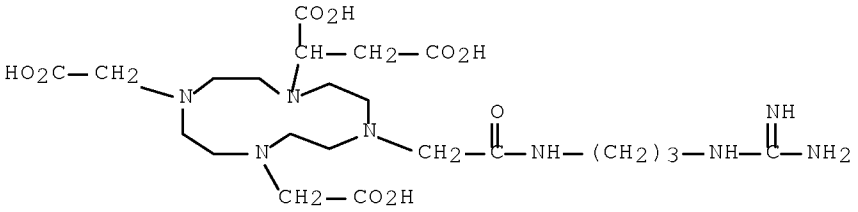
RN 849610-70-4 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(5-aminopentyl)amino]-2-oxoethyl]-α-(carboxymethyl)- (9CI) (CA INDEX NAME)



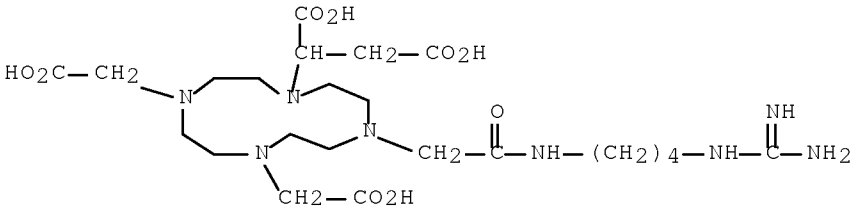
RN 849610-71-5 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-aminohexyl)amino]-2-oxoethyl]-α-(carboxymethyl)- (9CI) (CA INDEX NAME)



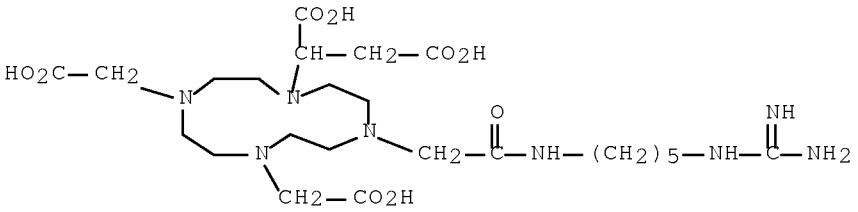
RN 849610-72-6 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[(aminoiminomethyl)amino]propyl]amino]-2-oxoethyl]-α-(carboxymethyl)- (9CI) (CA INDEX NAME)



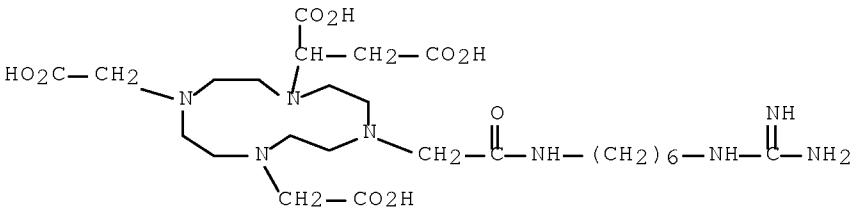
RN 849610-73-7 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[4-[(aminoiminomethyl)amino]butyl]amino]-2-oxoethyl]-α-(carboxymethyl)-(9CI) (CA INDEX NAME)



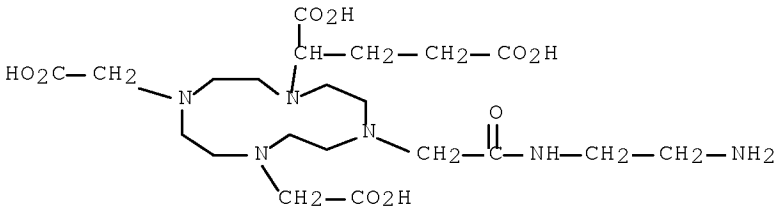
RN 849610-74-8 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[5-[(aminoiminomethyl)amino]pentyl]amino]-2-oxoethyl]-α-(carboxymethyl)-(9CI) (CA INDEX NAME)



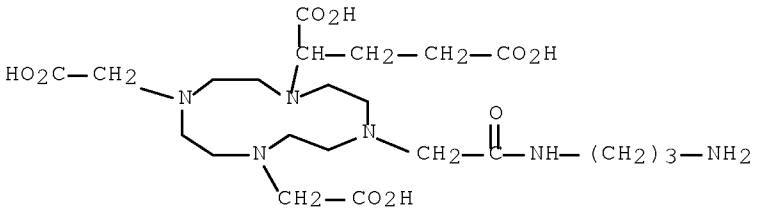
RN 849610-75-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[(aminoiminomethyl)amino]hexyl]amino]-2-oxoethyl]-α-(carboxymethyl)-(9CI) (CA INDEX NAME)



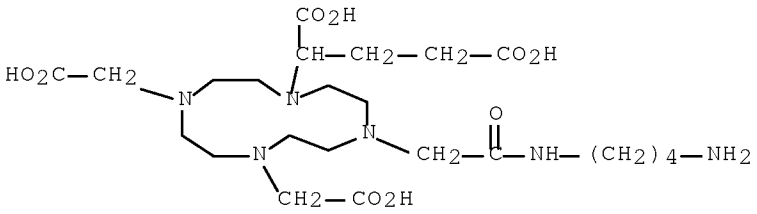
RN 849610-76-0 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-α-(2-carboxyethyl)- (CA INDEX NAME)



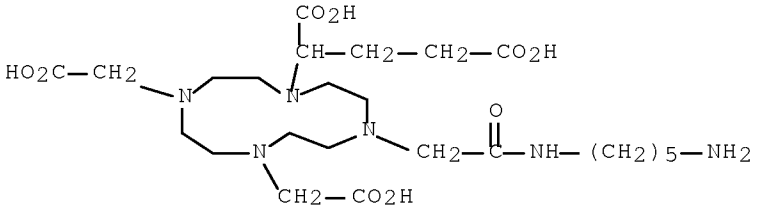
RN 849610-77-1 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(3-aminopropyl)amino]-2-oxoethyl]-α-(2-carboxyethyl)- (9CI) (CA INDEX NAME)



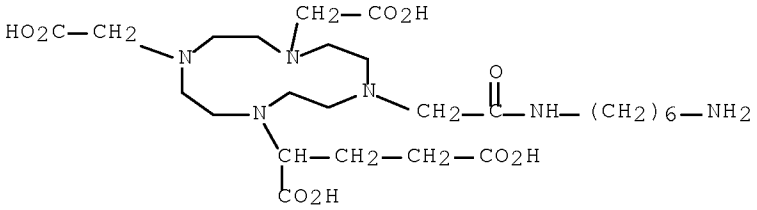
RN 849610-78-2 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(4-aminobutyl)amino]-2-oxoethyl]-α-(2-carboxyethyl)- (9CI) (CA INDEX NAME)



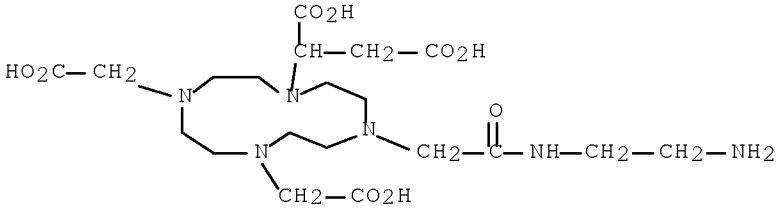
RN 849610-79-3 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(5-aminopentyl)amino]-2-oxoethyl]-α-(2-carboxyethyl)- (9CI) (CA INDEX NAME)



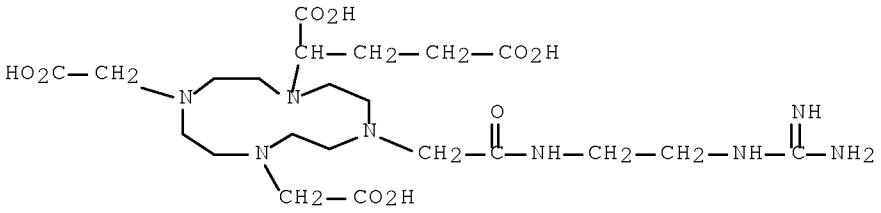
RN 849610-80-6 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-aminohexyl)amino]-2-oxoethyl]-α-(2-carboxyethyl)- (9CI) (CA INDEX NAME)



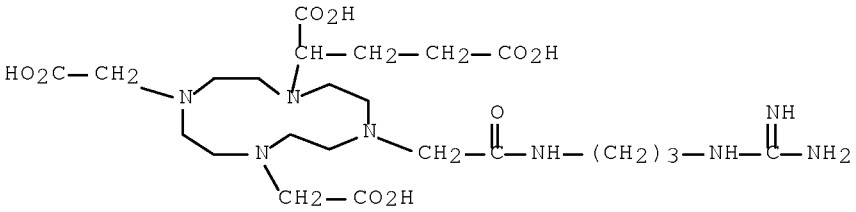
RN 849610-81-7 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-α-(carboxymethyl)- (9CI) (CA INDEX NAME)



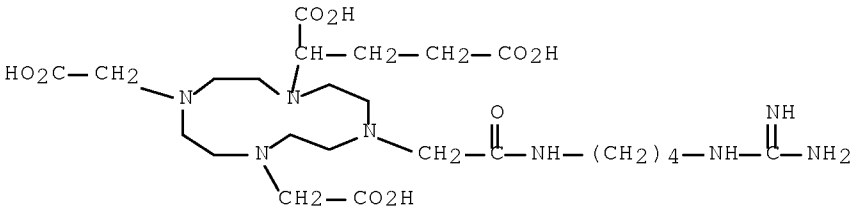
RN 849610-82-8 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[(aminoiminomethyl)amino]ethyl]amino]-2-oxoethyl]-α-(2-carboxyethyl)- (CA INDEX NAME)



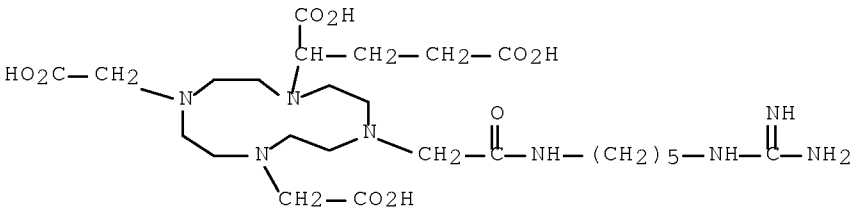
RN 849610-83-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[(aminoiminomethyl)amino]propyl]amino]-2-oxoethyl]-α-(2-carboxyethyl)- (CA INDEX NAME)



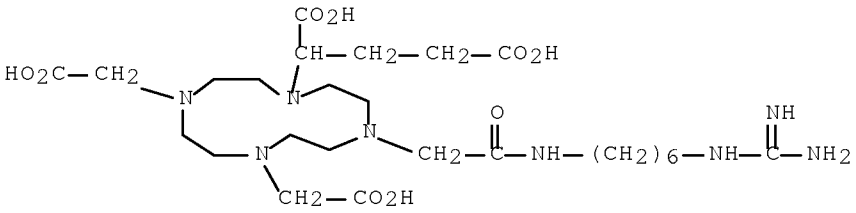
RN 849610-84-0 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[4-[(aminoiminomethyl)amino]butyl]amino]-2-oxoethyl]-α1-(2-carboxyethyl)- (9CI) (CA INDEX NAME)



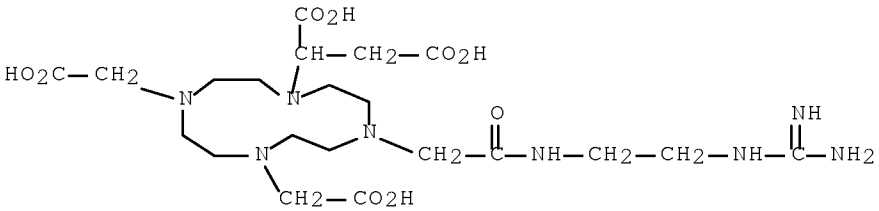
RN 849610-85-1 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[5-[(aminoiminomethyl)amino]pentyl]amino]-2-oxoethyl]-α1-(2-carboxyethyl)- (9CI) (CA INDEX NAME)



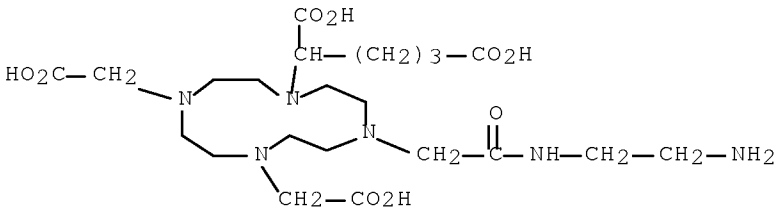
RN 849610-86-2 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[(aminoiminomethyl)amino]hexyl]amino]-2-oxoethyl]-α1-(2-carboxyethyl)- (9CI) (CA INDEX NAME)



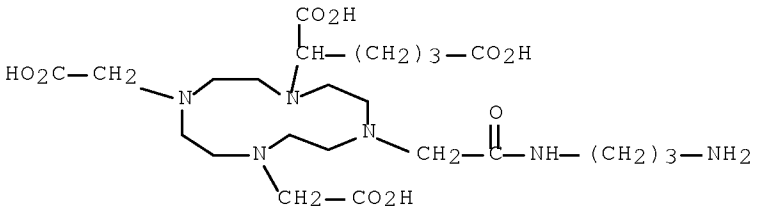
RN 849610-87-3 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[(aminoiminomethyl)amino]ethyl]amino]-2-oxoethyl]-α1-(carboxymethyl)- (9CI) (CA INDEX NAME)



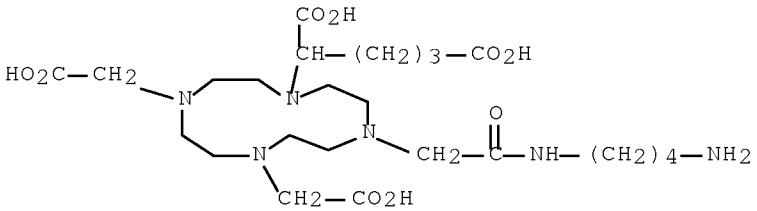
RN 849610-88-4 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-α1-(3-carboxypropyl)- (9CI) (CA INDEX NAME)



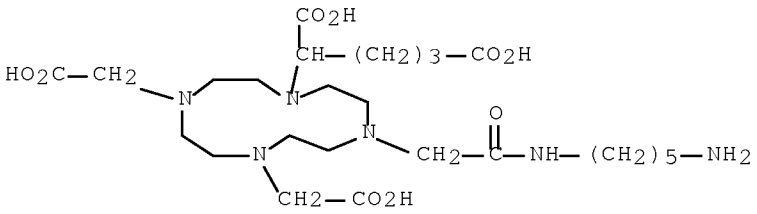
RN 849610-89-5 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(3-aminopropyl)amino]-2-oxoethyl]-α1-(3-carboxypropyl)- (9CI) (CA INDEX NAME)



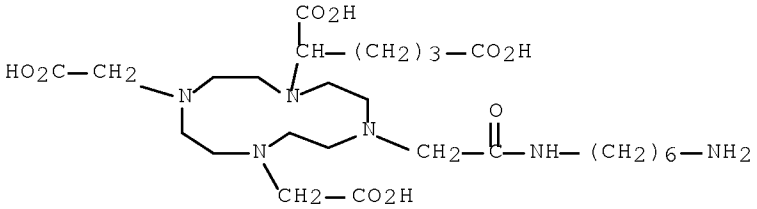
RN 849610-90-8 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(4-aminobutyl)amino]-2-oxoethyl]-α1-(3-carboxypropyl)- (9CI) (CA INDEX NAME)



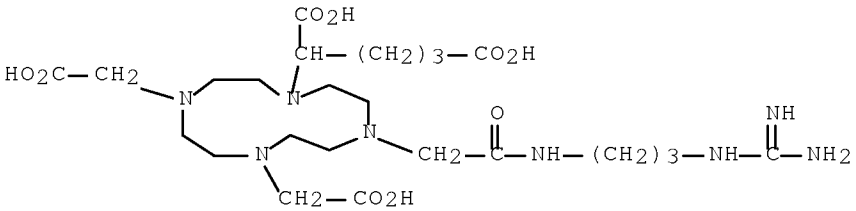
RN 849610-91-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(5-aminopentyl)amino]-2-oxoethyl]-α1-(3-carboxypropyl)- (CA INDEX NAME)



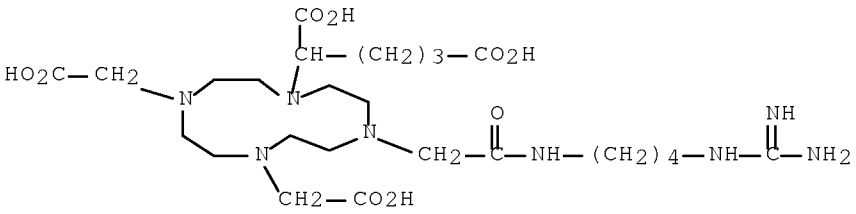
RN 849610-92-0 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-aminohexyl)amino]-2-oxoethyl]-α1-(3-carboxypropyl)- (9CI) (CA INDEX NAME)



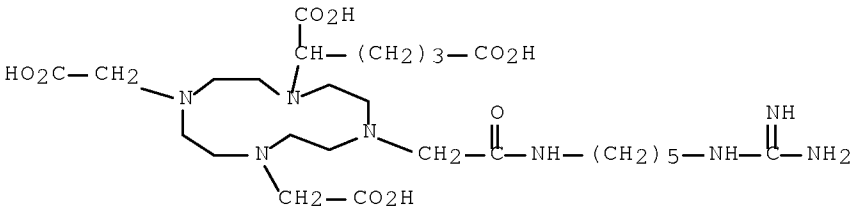
RN 849610-93-1 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[(aminoiminomethyl)amino]propyl]amino]-2-oxoethyl]-α1-(3-carboxypropyl)- (CA INDEX NAME)



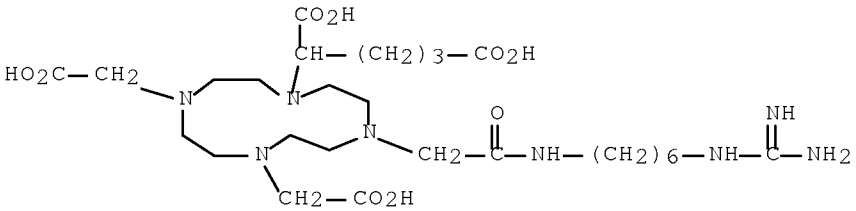
RN 849610-94-2 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[4-[(aminoiminomethyl)amino]butyl]amino]-2-oxoethyl]-α1-(3-carboxypropyl)- (CA INDEX NAME)



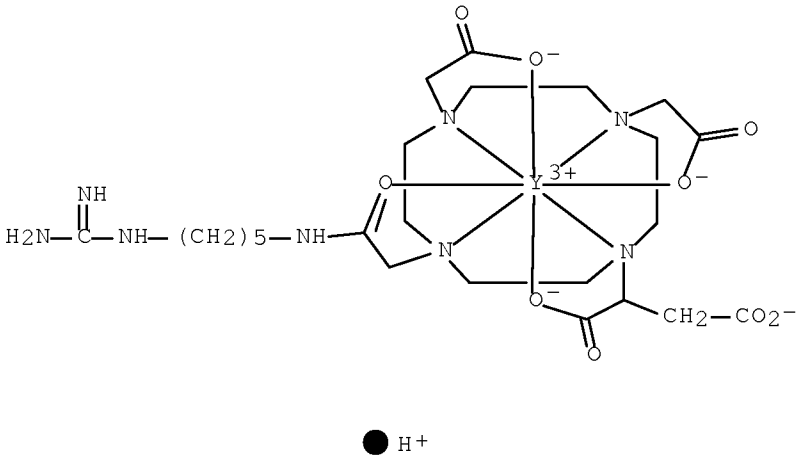
RN 849610-95-3 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[5-[(aminoiminomethyl)amino]pentyl]amino]-2-oxoethyl]-α1-(3-carboxypropyl)- (9CI) (CA INDEX NAME)



RN 849610-96-4 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[(aminoiminomethyl)amino]hexyl]amino]-2-oxoethyl]-α1-(3-carboxypropyl)- (9CI) (CA INDEX NAME)



RN 849680-88-2 ZCAPLUS
CN Yttrate(1-), [10-[2-[[5-[(aminoiminomethyl)amino]pentyl]amino]-2-(oxo-κO)ethyl]-α1-(carboxymethyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(5-)-κN1,κN4,κN7,κN10,κO1,.kappa.O4,κO7]-, hydrogen (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 2 OF 5 ZCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:878386 ZCAPLUS Full-text
DOCUMENT NUMBER: 141:366126
TITLE: Preparation of quaternized derivatives of (morpholinyl)phenylbenzopyranone as Pi-3 kinase inhibitor prodrugs
INVENTOR(S): Garlich, Joseph R.; Durden, Donald L.; Patterson, Mary; Su, Jingdong; Suhr, Robert G.
PATENT ASSIGNEE(S): Semafore Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089925	A1	20041021	WO 2004-US10399	20040403
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004228668	A1	20041021	AU 2004-228668	20040403
CA 2518916	A1	20041021	CA 2004-2518916	20040403
EP 1611119	A1	20060104	EP 2004-758869	20040403
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
BR 2004009063	A	20060328	BR 2004-9063	20040403
CN 1826331	A	20060830	CN 2004-80009226	20040403

JP 2006523237	T	20061012	JP 2006-509693		20040403
US 2004242631	A1	20041202	US 2004-818145		20040405
US 6949537	B2	20050927			
US 2005203173	A1	20050915	US 2005-111201		20050420
MX 2005PA10471	A	20060525	MX 2005-PA10471		20050929
KR 2007087266	A	20070828	KR 2005-718781		20050930
IN 2005DN04597	A	20070817	IN 2005-DN4597		20051010
PRIORITY APPLN. INFO.:			US 2003-460137P	P	20030403
			WO 2004-US10399	A	20040403
			US 2004-818145	A1	20040405

OTHER SOURCE(S): MARPAT 141:366126
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides methods to prepare prodrugs I [Z and Z1-3 independently = O or S; R1 and R2 independently = H, (un)substituted- aliphatic, -aryl, OH, CN, halo, etc.; R3 = H, (un)substituted-aliphatic, -aryl; R4 and R5 = H, (un)substituted-aliphatic, -aryl, heterocyclyl, aryloxy, carboxy, or taken together form an (un)substituted heterocycle; R6 = H, (un)substituted-aliphatic, -aryl, etc.; R7 = -CH2-, -CH(CH3)-, -CH(Ph)-, -C(CH3)(CO2H)- or CH(CH(CH3)2)-; T is optional but when present = targeting agent], possessing a hydrolyzable quaternary nitrogen which can provide metabolites II capable of inhibiting PI-3 kinase. Thus, e.g., III was prepared via N-alkylation of IV with chloromethyl-t-butylsuccinate followed by hydrolysis and chlorination to the acid chloride which was reacted with resin bound peptide (arg-gly-asp-ser) after which cleavage from the resin provided III. III was evaluated for in vivo efficacy against non-small cell lung cancer and after 17 days a 35% reduction in tumor volume was observed (at 25mg/kg/day dosage). The novel compds. are IV and analogs thereof comprising a reversibly quaternized amine.
IC ICM C07D311-22
ICS C07D407-12; C07D475-04; A61K031-5377; A61P025-00
CC 27-14 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 34, 63
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 3 OF 5 ZCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:891169 ZCAPLUS Full-text
DOCUMENT NUMBER: 142:322489
TITLE: Nanoparticles for delivery of pifithrins to combat cell death due to chemotherapy and radiation
AUTHOR(S): Brannon-Peppas, L.; Soehl, K.; Monaco, M. D.; Garlich, J.; Patterson, M.; Smith, T. C.
CORPORATE SOURCE: Department of Biomedical Engineering and Division of Pharmaceutics, The University of Texas at Austin, Austin, TX, 78712-0231, USA
SOURCE: Journal of Drug Delivery Science and Technology (2004), 14(4), 257-264
CODEN: JDDSAL
PUBLISHER: Editions de Sante
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This work describes the first stage of our research efforts to develop targetable nanoparticles to deliver agents to help healthy bone marrow cells survive radiation and chemotherapy. Administering pifithrin, a small mol. inhibitor of the protein p53, could prevent p53 initiated cell death. The p53

protein imparts sensitivity to normal tissue subjected to genotoxic stress such as radiation therapy or chemotherapy. We describe the conversion of pifithrin-α to pifithrin-β in buffer and serum and even while frozen and the implications in developing successful formulations. Encapsulation of pifithrin-β in biodegradable nanoparticles of poly(lactic-co-glycolic) acid showed encapsulation of up to 13% pifithrin and release in vitro of at least 28 days. Particle sizes ranged from 240 to 3250 nm, depending on the preparation methods used including variation of organic solvent type and amount

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 8

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 4 OF 5 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:435190 ZCAPLUS Full-text
TITLE: Targeted Delivery of p53 Inhibitors
AUTHOR(S): Smith, Tim C.; Garlich, Joseph R.; Patterson, Mary L.; Suhr, Robert G.
CORPORATE SOURCE: Semafore Pharmaceuticals, Indianapolis, IN, 46268, USA
SOURCE: Abstracts, 36th Central Regional Meeting of the American Chemical Society, Indianapolis, IN, United States, June 2-4 (2004), GEN-452. American Chemical Society: Washington, D. C.
CODEN: 69FMAU
DOCUMENT TYPE: Conference; Meeting Abstract

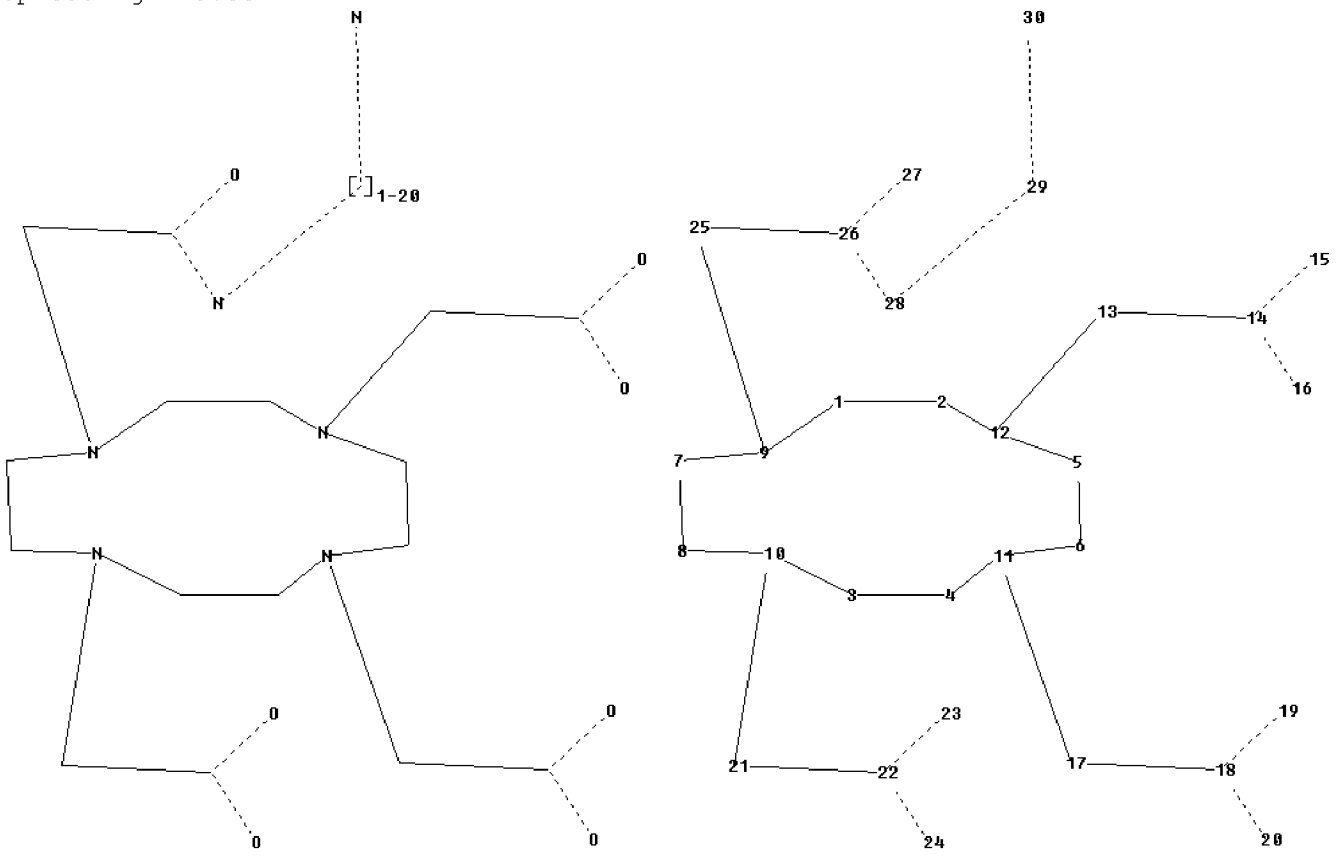
AB The protein p53 is a tumor suppressor, which often is triggered during chemo- and radiation therapy, causing unwanted side effects by inducing apoptosis of healthy tissue such as the hematopoietic system. Thus suppression of p53 in healthy tissues during therapy should decrease the damage. Pifithrin- and pifithrin- have been shown to act as small mol. inhibitors of p53. We have embarked on a program to target pifithrin- and to bone, thus offering selective protection to bone marrow and the immune system during therapy. This presentation will focus on the synthetic chemical of linking bone-seeking moieties to pifithrin- and as well as promising preliminary in vitro studies.

L78 ANSWER 5 OF 5 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:435232 ZCAPLUS Full-text
TITLE: Novel Purification Techniques and the Solid Phase Synthesis of Macrocyclic Ligands
AUTHOR(S): Garlich, Joseph R.; Patterson, Mary; Smith, Tim C.; Suhr, Robert G.; Georgiadis, Taxiarchis M.
CORPORATE SOURCE: Semafore Pharmaceuticals, Indianapolis, IN, 46268, USA
SOURCE: Abstracts, 36th Central Regional Meeting of the American Chemical Society, Indianapolis, IN, United States, June 2-4 (2004), INV-033. American Chemical Society: Washington, D. C.
CODEN: 69FMAU
DOCUMENT TYPE: Conference; Meeting Abstract

AB One highly useful procedure in parallel or combinatorial synthesis is the clean-up of reaction mixts. using facilitated liquid-liquid extraction Researchers have previously described the use of large mesh sized diatomaceous earth beads coated with an aqueous phase for simultaneous extraction workup of an array of compds. simply by exposure of the reaction mix dissolved in an organic phase to the beads. We have taken this concept beyond simple liquid-liquid extns. by employing diatomaceous earth beads coated with various aqueous based scavenging, catalytic and reactive solns. This supported aqueous film exposure can be utilized during a reaction to introduce catalysts or reactive reagents which react at the films water-organic interface. Post-

reaction workup is thus reduced to simple filtration or decanting. Novel phys. formats for this technique have also been explored. This work and the solid-phase synthesis of macrocyclic ligands will be discussed.

```
=> file registry
FILE 'REGISTRY' ENTERED AT 10:22:51 ON 21 FEB 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   20 FEB 2008  HIGHEST RN 1004854-20-9
DICTIONARY FILE UPDATES:  20 FEB 2008  HIGHEST RN 1004854-20-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

Uploading L25.str
```

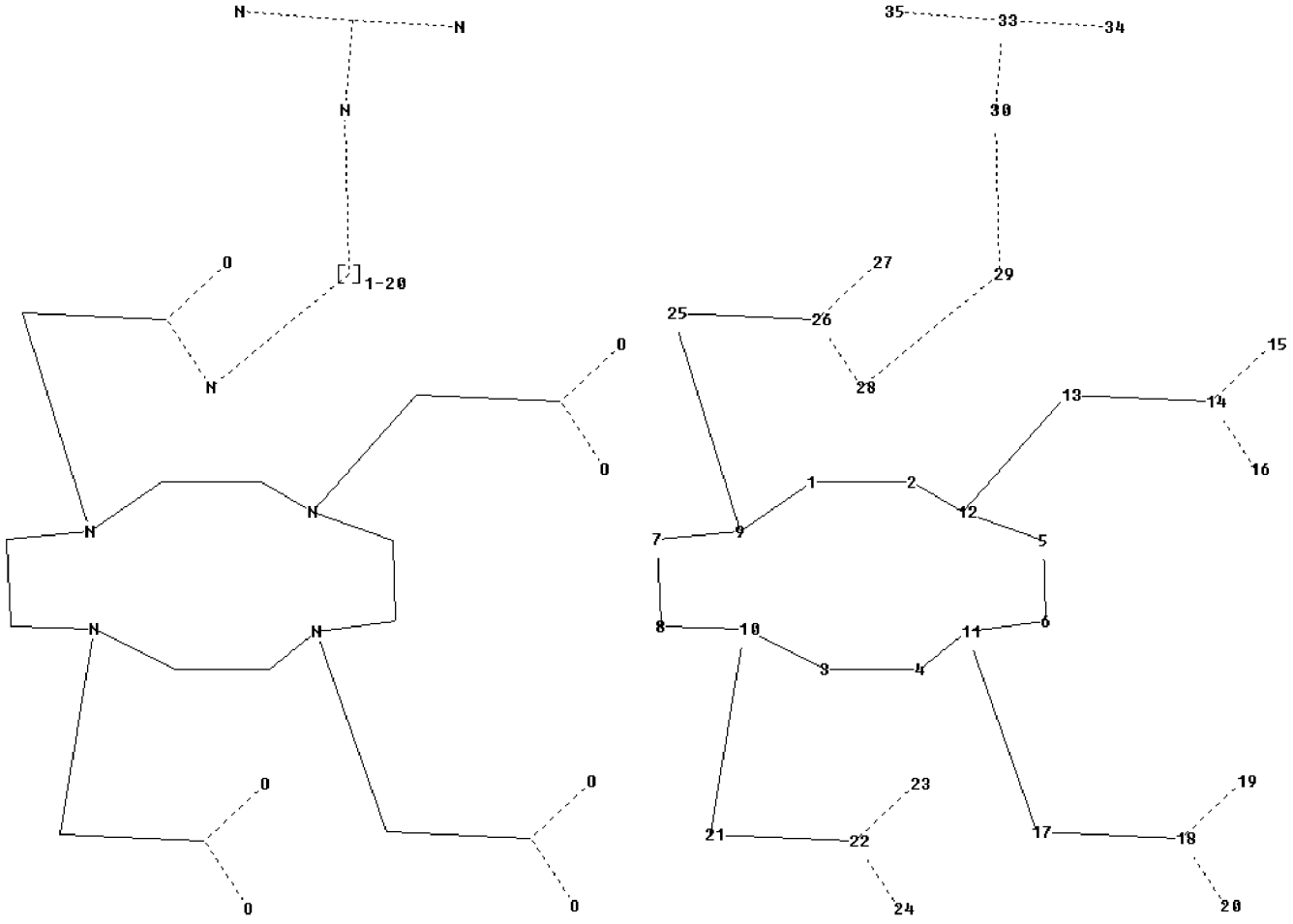



```
ring nodes :
```

1 2 3 4 5 6 7 8 9 10 11 12
ring/chain nodes :
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
ring/chain bonds :
9-25 10-21 11-17 12-13 13-14 14-16 14-15 17-18 18-20 18-19 21-22 22-24
22-23 25-26 26-28 26-27 28-29 29-30
ring bonds :
1-2 1-9 2-12 3-4 3-10 4-11 5-6 5-12 6-11 7-8 7-9 8-10
exact/norm bonds :
1-2 1-9 2-12 3-4 3-10 4-11 5-6 5-12 6-11 7-8 7-9 8-10 9-25 10-21 11-
17
12-13 13-14 14-16 14-15 17-18 18-20 18-19 21-22 22-24 22-23 25-26 26-28
26-27 28-29
29-30

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS
22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS
30:CLASS

Uploading L27.str

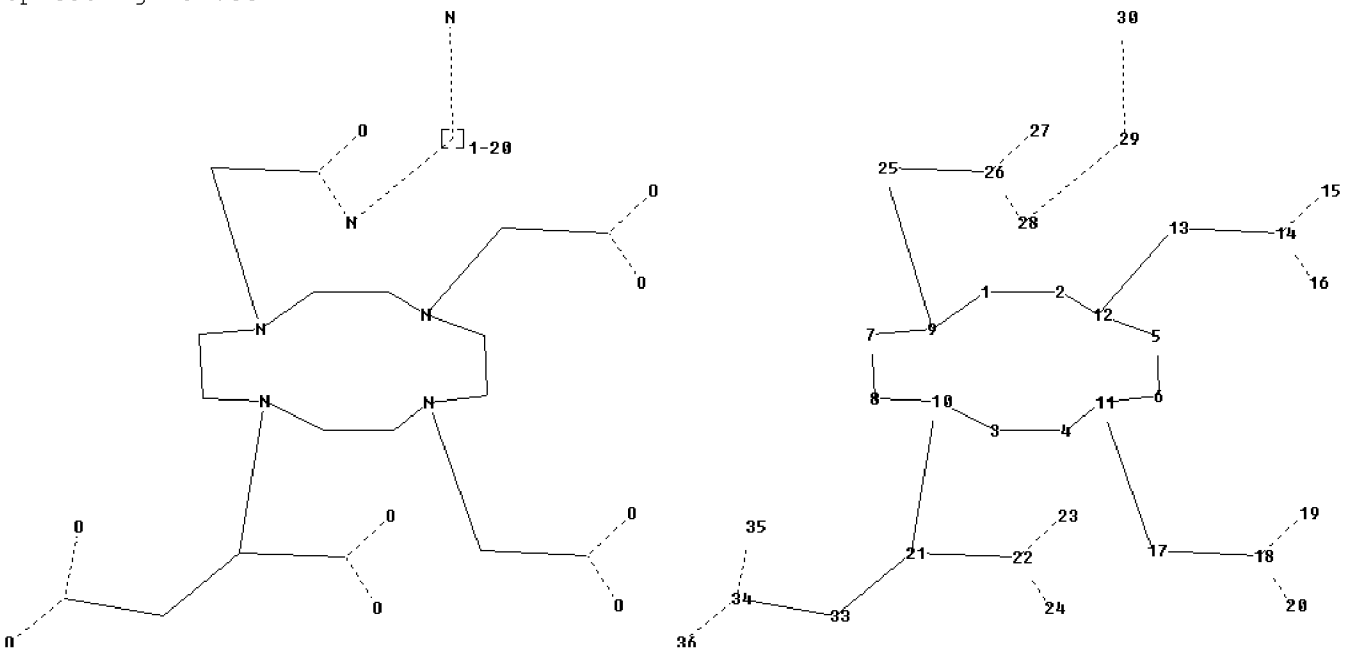


ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
ring/chain nodes :
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 33 34 35

ring/chain bonds :
9-25 10-21 11-17 12-13 13-14 14-16 14-15 17-18 18-20 18-19 21-22 22-24
22-23 25-26 26-28 26-27 28-29 29-30 30-33 33-34 33-35
ring bonds :
1-2 1-9 2-12 3-4 3-10 4-11 5-6 5-12 6-11 7-8 7-9 8-10
exact/norm bonds :
1-2 1-9 2-12 3-4 3-10 4-11 5-6 5-12 6-11 7-8 7-9 8-10 9-25 10-21 11-
17
12-13 13-14 14-16 14-15 17-18 18-20 18-19 21-22 22-24 22-23 25-26 26-28
26-27 28-29
29-30 30-33 33-34 33-35

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS
22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS
30:CLASS
33:CLASS 34:CLASS 35:CLASS

Uploading L34.str

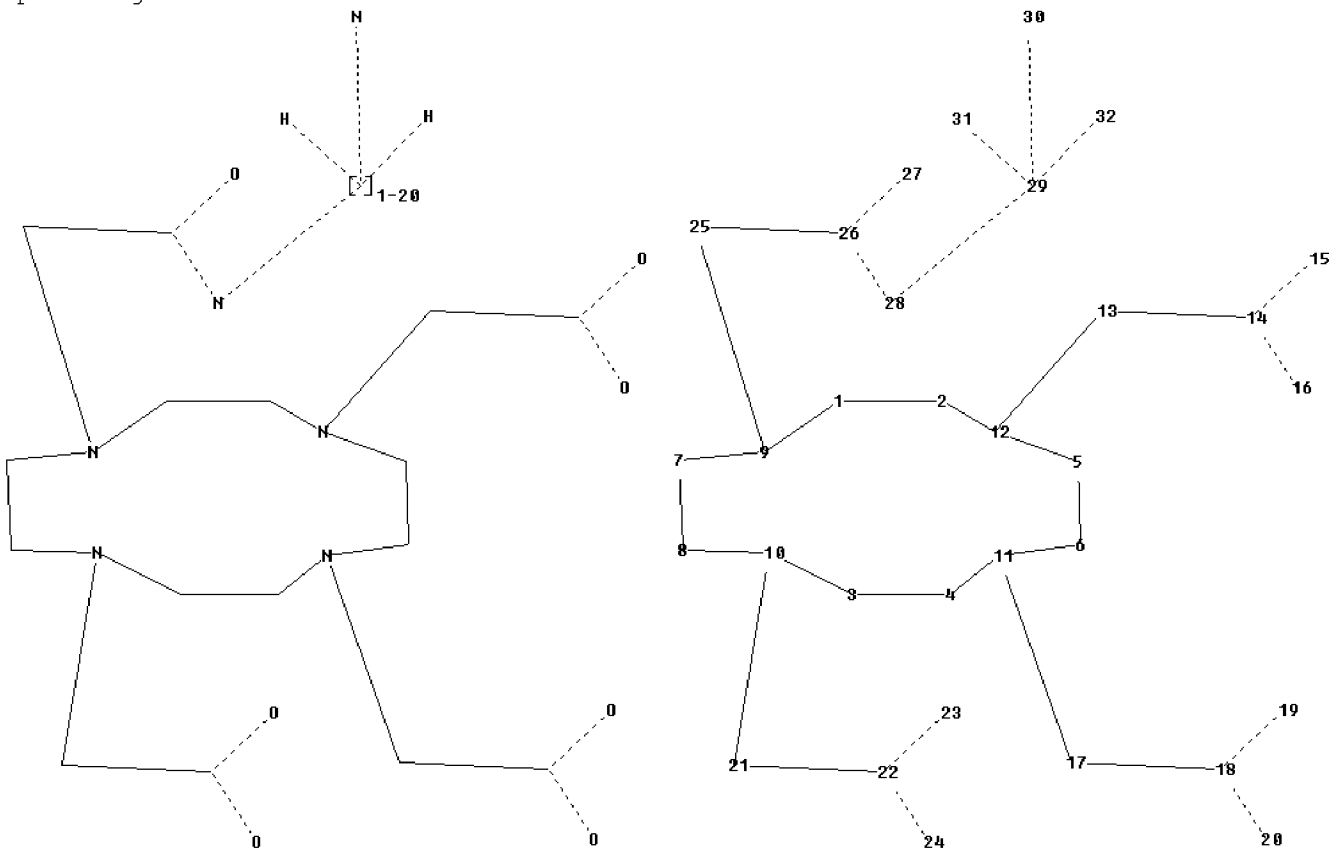


ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
ring/chain nodes :
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 33 34 35
36
ring/chain bonds :
9-25 10-21 11-17 12-13 13-14 14-16 14-15 17-18 18-20 18-19 21-22 21-33

22-24 22-23 25-26 26-28 26-27 28-29 29-30 33-34 34-35 34-36
ring bonds :
1-2 1-9 2-12 3-4 3-10 4-11 5-6 5-12 6-11 7-8 7-9 8-10
exact/norm bonds :
1-2 1-9 2-12 3-4 3-10 4-11 5-6 5-12 6-11 7-8 7-9 8-10 9-25 10-21 11-17
12-13 13-14 14-16 14-15 17-18 18-20 18-19 21-22 21-33 22-24 22-23 25-26 26-28 26-27
28-29 29-30 33-34 34-35 34-36

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS
22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS
30:CLASS
33:CLASS 34:CLASS 35:CLASS 36:CLASS

Uploading L47.str



chain nodes :
31 32
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
ring/chain nodes :
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
chain bonds :
29-31 29-32

```
ring/chain bonds :
9-25  10-21  11-17  12-13  13-14  14-16  14-15  17-18  18-20  18-19  21-22  22-24
22-23  25-26  26-28  26-27  28-29  29-30
ring bonds :
1-2  1-9  2-12  3-4  3-10  4-11  5-6  5-12  6-11  7-8  7-9  8-10
exact/norm bonds :
1-2  1-9  2-12  3-4  3-10  4-11  5-6  5-12  6-11  7-8  7-9  8-10  9-25  10-21  11-
17
12-13  13-14  14-16  14-15  17-18  18-20  18-19  21-22  22-24  22-23  25-26  26-28
26-27  28-29
29-30  29-31  29-32


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS
19:CLASS  20:CLASS  21:CLASS
22:CLASS  23:CLASS  24:CLASS  25:CLASS  26:CLASS  27:CLASS  28:CLASS  29:CLASS
30:CLASS
31:CLASS  32:CLASS



=> file zcaplus
FILE 'ZCAPLUS' ENTERED AT 10:22:54 ON 21 FEB 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS is
strictly prohibited.

FILE COVERS 1907 - 21 Feb 2008  VOL 148 ISS 8
FILE LAST UPDATED: 20 Feb 2008  (20080220/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

=> d stat que L32
L25             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L27             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *
```

```
Structure attributes must be viewed using STN Express query preparation.
L29        2020 SEA FILE=REGISTRY SSS FUL L25
L31          62 SEA FILE=REGISTRY SUB=L29 SSS FUL L27
L32           9 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L31


=> d stat que L37
L25             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L29        2020 SEA FILE=REGISTRY SSS FUL L25
L34             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L36          12 SEA FILE=REGISTRY SUB=L29 SSS FUL L34
L37           1 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L36


=> d stat que L45
L2            65 SEA FILE=REGISTRY ABB=ON  PLU=ON  (118726-52-6/BI OR 17137-11-0
                 /BI OR 294-90-6/BI OR 507475-91-4/BI OR 5292-43-3/BI OR
                 7429-91-6/BI OR 7439-91-0/BI OR 7439-94-3/BI OR 7440-00-8/BI
                 OR 7440-10-0/BI OR 7440-12-2/BI OR 7440-19-9/BI OR 7440-20-2/BI
                  OR 7440-27-9/BI OR 7440-30-4/BI OR 7440-45-1/BI OR 7440-52-0/B
                 I OR 7440-53-1/BI OR 7440-54-2/BI OR 7440-60-0/BI OR 7440-64-4/
                 BI OR 7440-65-5/BI OR 849610-60-2/BI OR 849610-61-3/BI OR
                 849610-62-4/BI OR 849610-63-5/BI OR 849610-64-6/BI OR 849610-65
                 -7/BI OR 849610-66-8/BI OR 849610-67-9/BI OR 849610-68-0/BI OR
                 849610-69-1/BI OR 849610-70-4/BI OR 849610-71-5/BI OR 849610-72
                 -6/BI OR 849610-73-7/BI OR 849610-74-8/BI OR 849610-75-9/BI OR
                 849610-76-0/BI OR 849610-77-1/BI OR 849610-78-2/BI OR 849610-79
                 -3/BI OR 849610-80-6/BI OR 849610-81-7/BI OR 849610-82-8/BI OR
                 849610-83-9/BI OR 849610-84-0/BI OR 849610-85-1/BI OR 849610-86
                 -2/BI OR 849610-87-3/BI OR 849610-88-4/BI OR 849610-89-5/BI OR
                 849610-90-8/BI OR 849610-91-9/BI OR 849610-92-0/BI OR 849610-93
                 -1/BI OR 849610-94-2/BI OR 849610-95-3/BI OR 849610-96-4/BI OR
                 849610-97-5/BI OR 849610-98-6/BI OR 849610-99-7/BI OR 849611-00
                 -3/BI OR 849680-88-2/BI OR 95196-95-5/BI)
L25             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L27             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L29        2020 SEA FILE=REGISTRY SSS FUL L25
L31          62 SEA FILE=REGISTRY SUB=L29 SSS FUL L27
L32           9 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L31
L34             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
```

```
L36          12 SEA FILE=REGISTRY SUB=L29 SSS FUL L34
L37           1 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L36
L38           9 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L37 OR L32
L40         273 SEA FILE=REGISTRY ABB=ON  PLU=ON  (934183-16-1/BI OR 111119-28-
                9/BI OR 137076-54-1/BI OR 14265-75-9/BI OR 15750-15-9/BI OR
                15757-14-9/BI OR 317809-26-0/BI OR 33507-63-0/BI OR 705283-66-5
                /BI OR 901439-51-8/BI OR 901439-89-2/BI OR 901442-07-7/BI OR
                901443-47-8/BI OR 91037-65-9/BI OR 934183-14-9/BI OR 934183-15-
                0/BI OR 934350-78-4/BI OR 934350-82-0/BI OR 934350-86-4/BI OR
                934350-87-5/BI OR 10098-91-6/BI OR 110880-55-2/BI OR 110880-57-
                4/BI OR 111844-19-0/BI OR 112188-16-6/BI OR 115608-61-2/BI OR
                118726-52-6/BI OR 128009-23-4/BI OR 135702-31-7/BI OR 137184-55
                -5/BI OR 137813-35-5/BI OR 13967-64-1/BI OR 13967-65-2/BI OR
                13981-25-4/BI OR 13981-56-1/BI OR 14119-08-5/BI OR 14119-09-6/B
                I OR 14133-76-7/BI OR 141743-95-5/BI OR 14191-64-1/BI OR
                14265-85-1/BI OR 14687-25-3/BI OR 14809-53-1/BI OR 14834-85-6/B
                I OR 14885-78-0/BI OR 148893-10-1/BI OR 14913-49-6/BI OR
                14981-79-4/BI OR 15065-93-7/BI OR 15757-86-5/BI OR 15765-31-8/B
                I OR 15776-20-2/BI OR 161552-03-0/BI OR 17137-11-0/BI OR
                174267-75-5/BI OR 188982-12-9/BI OR 22541-18-0/BI OR 22541-19-1
                /BI OR 267410-13-9/BI OR 29022-11-5/BI OR 294-90-6/BI OR
                36849-05-5/BI OR 41444-88-6/BI OR 415706-07-9/BI OR 507475-91-4
                /BI OR 5292-43-3/BI OR 585531-74-4/BI OR 6066-82-6/BI OR
                623575-85-9/BI OR 676544-84-6/BI OR 676544-85-7/BI OR 676553-18
                -7/BI OR 676553-19-8/BI OR 7087-68-5/BI OR 713520-27-5/BI OR
                728914-72-5/BI OR 728914-74-7/BI OR 7429-91-6/BI OR 7439-91-0/B
                I OR 7439-94-3/BI OR 7440-00-8/BI OR 7440-10-0/BI OR 7440-12-2/
                BI OR 7440-19-9/BI OR 7440-20-2/BI OR 7440-27-9/BI OR 7440-30-4
                /BI OR 7440-45-1/BI OR 7440-52-0/BI OR 7440-53-1/BI OR
                7440-54-2/BI OR 7440-60-0/BI OR 7440-64-4/BI OR 7440-65-5/BI
                OR 766529-14-0/BI OR 766529-15-1/BI OR 766529-16-2/BI OR
                766529-18-4/BI OR 766529-19-5/BI OR 766529-20-8/BI OR 766529-22
                -0/BI OR 766529-24-2/BI OR 766529-25-3/BI OR 76652
L41          65 SEA FILE=REGISTRY ABB=ON  PLU=ON  L40 AND L2
L42          75 SEA FILE=REGISTRY ABB=ON  PLU=ON  L40 AND M/ELS
L45           8 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  (L41 OR L42) AND L38


=> d stat que L55
L25             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L29        2020 SEA FILE=REGISTRY SSS FUL L25
L47             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L49         345 SEA FILE=REGISTRY SUB=L29 SSS FUL L47
L50         142 SEA FILE=REGISTRY ABB=ON  PLU=ON  L49 AND M/ELS
L54           9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L50 AND Y/ELS
L55          10 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L54


=> d stat que L67
L2           65 SEA FILE=REGISTRY ABB=ON  PLU=ON  (118726-52-6/BI OR 17137-11-0
                /BI OR 294-90-6/BI OR 507475-91-4/BI OR 5292-43-3/BI OR
                7429-91-6/BI OR 7439-91-0/BI OR 7439-94-3/BI OR 7440-00-8/BI
```

```
                OR 7440-10-0/BI OR 7440-12-2/BI OR 7440-19-9/BI OR 7440-20-2/BI
                 OR 7440-27-9/BI OR 7440-30-4/BI OR 7440-45-1/BI OR 7440-52-0/B
                I OR 7440-53-1/BI OR 7440-54-2/BI OR 7440-60-0/BI OR 7440-64-4/
                BI OR 7440-65-5/BI OR 849610-60-2/BI OR 849610-61-3/BI OR
                849610-62-4/BI OR 849610-63-5/BI OR 849610-64-6/BI OR 849610-65
                -7/BI OR 849610-66-8/BI OR 849610-67-9/BI OR 849610-68-0/BI OR
                849610-69-1/BI OR 849610-70-4/BI OR 849610-71-5/BI OR 849610-72
                -6/BI OR 849610-73-7/BI OR 849610-74-8/BI OR 849610-75-9/BI OR
                849610-76-0/BI OR 849610-77-1/BI OR 849610-78-2/BI OR 849610-79
                -3/BI OR 849610-80-6/BI OR 849610-81-7/BI OR 849610-82-8/BI OR
                849610-83-9/BI OR 849610-84-0/BI OR 849610-85-1/BI OR 849610-86
                -2/BI OR 849610-87-3/BI OR 849610-88-4/BI OR 849610-89-5/BI OR
                849610-90-8/BI OR 849610-91-9/BI OR 849610-92-0/BI OR 849610-93
                -1/BI OR 849610-94-2/BI OR 849610-95-3/BI OR 849610-96-4/BI OR
                849610-97-5/BI OR 849610-98-6/BI OR 849610-99-7/BI OR 849611-00
                -3/BI OR 849680-88-2/BI OR 95196-95-5/BI)
L25             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L27             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L29        2020 SEA FILE=REGISTRY SSS FUL L25
L31          62 SEA FILE=REGISTRY SUB=L29 SSS FUL L27
L32           9 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L31
L34             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L36          12 SEA FILE=REGISTRY SUB=L29 SSS FUL L34
L37           1 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L36
L38           9 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L37 OR L32
L40         273 SEA FILE=REGISTRY ABB=ON  PLU=ON  (934183-16-1/BI OR 111119-28-
                9/BI OR 137076-54-1/BI OR 14265-75-9/BI OR 15750-15-9/BI OR
                15757-14-9/BI OR 317809-26-0/BI OR 33507-63-0/BI OR 705283-66-5
                /BI OR 901439-51-8/BI OR 901439-89-2/BI OR 901442-07-7/BI OR
                901443-47-8/BI OR 91037-65-9/BI OR 934183-14-9/BI OR 934183-15-
                0/BI OR 934350-78-4/BI OR 934350-82-0/BI OR 934350-86-4/BI OR
                934350-87-5/BI OR 10098-91-6/BI OR 110880-55-2/BI OR 110880-57-
                4/BI OR 111844-19-0/BI OR 112188-16-6/BI OR 115608-61-2/BI OR
                118726-52-6/BI OR 128009-23-4/BI OR 135702-31-7/BI OR 137184-55
                -5/BI OR 137813-35-5/BI OR 13967-64-1/BI OR 13967-65-2/BI OR
                13981-25-4/BI OR 13981-56-1/BI OR 14119-08-5/BI OR 14119-09-6/B
                I OR 14133-76-7/BI OR 141743-95-5/BI OR 14191-64-1/BI OR
                14265-85-1/BI OR 14687-25-3/BI OR 14809-53-1/BI OR 14834-85-6/B
                I OR 14885-78-0/BI OR 148893-10-1/BI OR 14913-49-6/BI OR
                14981-79-4/BI OR 15065-93-7/BI OR 15757-86-5/BI OR 15765-31-8/B
                I OR 15776-20-2/BI OR 161552-03-0/BI OR 17137-11-0/BI OR
                174267-75-5/BI OR 188982-12-9/BI OR 22541-18-0/BI OR 22541-19-1
                /BI OR 267410-13-9/BI OR 29022-11-5/BI OR 294-90-6/BI OR
                36849-05-5/BI OR 41444-88-6/BI OR 415706-07-9/BI OR 507475-91-4
                /BI OR 5292-43-3/BI OR 585531-74-4/BI OR 6066-82-6/BI OR
                623575-85-9/BI OR 676544-84-6/BI OR 676544-85-7/BI OR 676553-18
                -7/BI OR 676553-19-8/BI OR 7087-68-5/BI OR 713520-27-5/BI OR
                728914-72-5/BI OR 728914-74-7/BI OR 7429-91-6/BI OR 7439-91-0/B
```

```
                I OR 7439-94-3/BI OR 7440-00-8/BI OR 7440-10-0/BI OR 7440-12-2/
                BI OR 7440-19-9/BI OR 7440-20-2/BI OR 7440-27-9/BI OR 7440-30-4
                /BI OR 7440-45-1/BI OR 7440-52-0/BI OR 7440-53-1/BI OR
                7440-54-2/BI OR 7440-60-0/BI OR 7440-64-4/BI OR 7440-65-5/BI
                OR 766529-14-0/BI OR 766529-15-1/BI OR 766529-16-2/BI OR
                766529-18-4/BI OR 766529-19-5/BI OR 766529-20-8/BI OR 766529-22
                -0/BI OR 766529-24-2/BI OR 766529-25-3/BI OR 76652
L41           65 SEA FILE=REGISTRY ABB=ON  PLU=ON  L40 AND L2
L42           75 SEA FILE=REGISTRY ABB=ON  PLU=ON  L40 AND M/ELS
L45            8 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  (L41 OR L42) AND L38
L47               STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L49          345 SEA FILE=REGISTRY SUB=L29 SSS FUL L47
L50          142 SEA FILE=REGISTRY ABB=ON  PLU=ON  L49 AND M/ELS
L51          203 SEA FILE=REGISTRY ABB=ON  PLU=ON  L49 NOT L50
L54            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L50 AND Y/ELS
L55           10 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L54
L56          112 SEA FILE=REGISTRY ABB=ON  PLU=ON  L50 AND LNTH/PG
L58           18 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  L32 OR L37 OR L45 OR L55
L60       641196 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  ?TUMOUR?/BI OR ?TUMOR?/BI
L62        25232 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  ?SCAFFOLD?/BI
L64            2 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  (L51 OR L56) AND L62
L65           40 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  (L51 OR L56) AND L60
L67            8 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  (L64 OR L65) AND L58


=> s (l32 or L37 or L45 or L55 or L67) not L73-L74
L79           17 (L32 OR L37 OR L45 OR L55 OR L67) NOT (L73 OR L74)

=> d ibib abs hitind hitstr L79 1-17

L79  ANSWER 1 OF 17  ZCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2007:1302637  ZCAPLUS  Full-text
DOCUMENT NUMBER:          147:522590
TITLE:                    Preparation of peptides containing the
                          D-Phe-D-Phe-D-Val-D-Leu-D-Lys sequence as imaging
                          agents
INVENTOR(S):              Austen, Brian
PATENT ASSIGNEE(S):       St. George's Hospital Medical School, UK
SOURCE:                   PCT Int. Appl., 36pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2007129077         A2    20071115    WO 2007-GB1669          20070504
     WO 2007129077         A3    20080103
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB,
             GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM,
             KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK,
             MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO,
             RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT,
             TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
```

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: GB 2006-8960 A 20060505

AB The invention relates to synthetic peptides capable of recognizing and binding to β-amyloid and to the use of the peptides in the diagnosis, monitoring and therapy of Alzheimer's disease (AD). Peptides containing the sequence D-Phe-D-Phe-D-Val-D-Leu-D-Lys (ffvlk) and an amine or guanidine substituent are claimed for this purpose. Thus, acetyl-rGffvlkr-NH2 and DOTA-rGffvlkGrG-pentadiamine (DOTA = 1,4,7,10-tetraazacyclododecane- 1,4,7,10-tetraacetic acid) Gd complex were prepared by the solid-phase method and assayed for inhibition of β-amyloid oligomer formation.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 78

IT 956489-86-4P 956599-09-0P 956599-10-3P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides containing D-configurated phenylalanylphenylalanylvalyl
leucylleucine sequence as imaging agents)

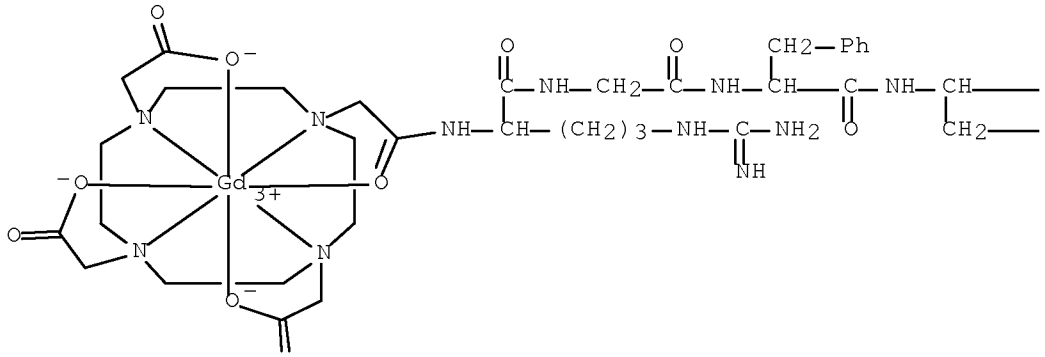
IT 956489-89-7P 956489-91-1P 956489-93-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides containing D-configurated phenylalanylphenylalanylvalyl
leucylleucine sequence as imaging agents)

IT 956599-09-0P 956599-10-3P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides containing D-configurated phenylalanylphenylalanylvalyl
leucylleucine sequence as imaging agents)

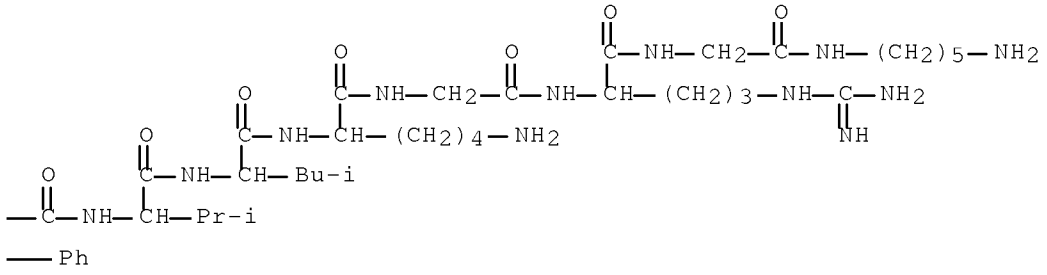
RN 956599-09-0 ZCAPLUS

CN Gadolinium, [N-[2-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetrazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-D-arginylglycyl-D-phenylalanyl-D-phenylalanyl-D-valyl-D-leucyl-D-lysylglycyl-D-arginyl-N-(5-aminopentyl)glycinamidato(3-)]- (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

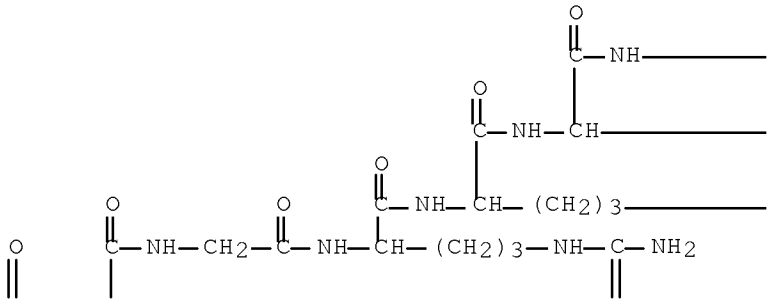


PAGE 2-A

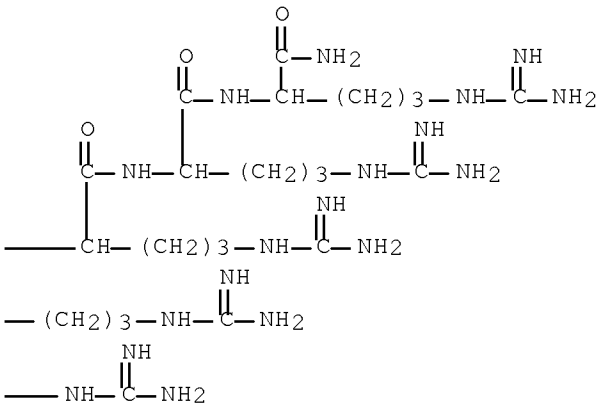
RN 956599-10-3 ZCAPLUS

CN Gadolinium, [N-[2-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetrazadodec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-D-arginylglycyl-D-phenylalanyl-D-phenylalanyl-D-valyl-D-leucyl-D-lysylglycyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl-D-argininamidato(3-)]- (CA INDEX NAME)

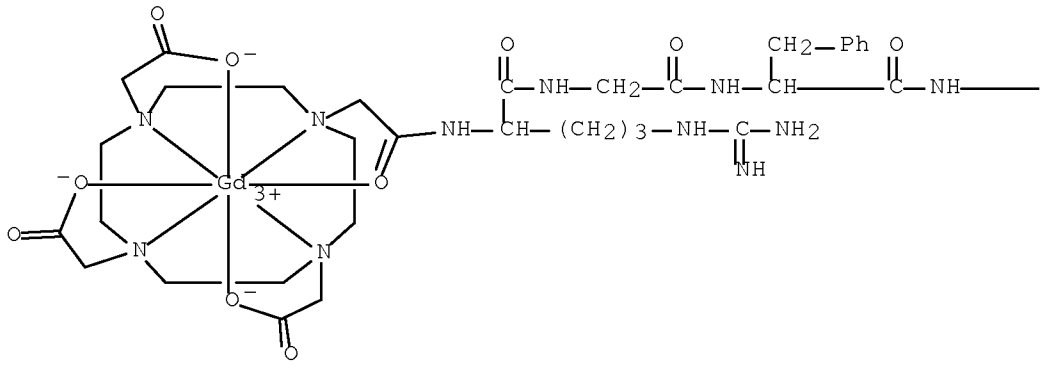
PAGE 1-B



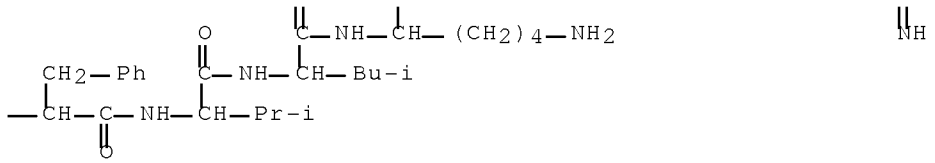
PAGE 1-C



PAGE 2-A



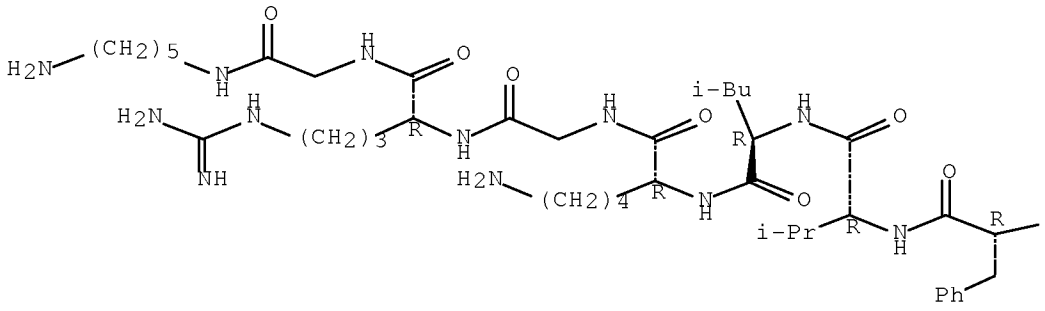
PAGE 2-B



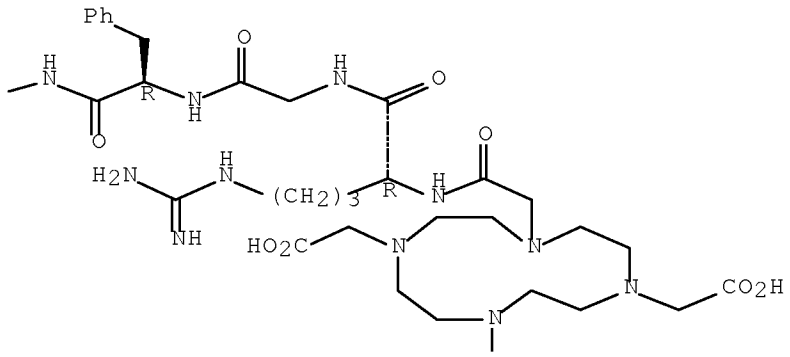
IT 956489-91-1P 956489-93-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides containing D-configurated phenylalanylphenylalanylvalyl
leucylleucine sequence as imaging agents)
RN 956489-91-1 ZCAPLUS
CN Glycinamide, N2-[2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-D-arginylglycyl-D-phenylalanyl-D-phenylalanyl-D-valyl-D-leucyl-D-lysylglycyl-D-arginyl-N-(5-aminopentyl)- (CA INDEX NAME)

Absolute stereochemistry.

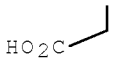
PAGE 1-A



PAGE 1-B



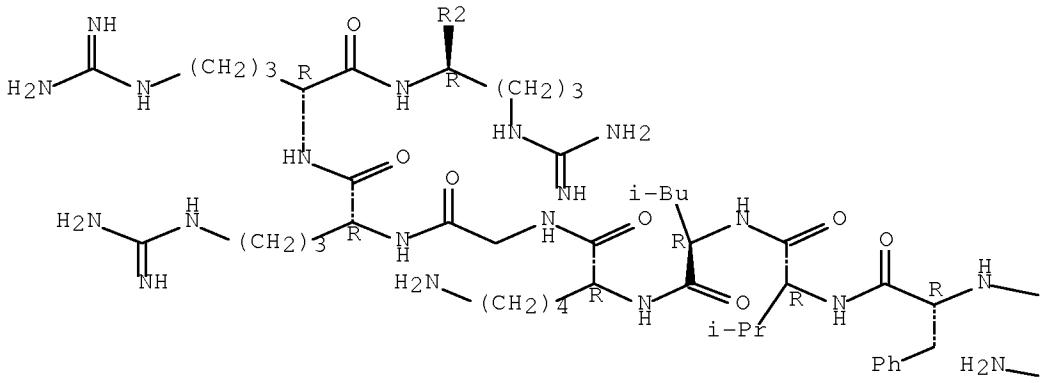
PAGE 2-B



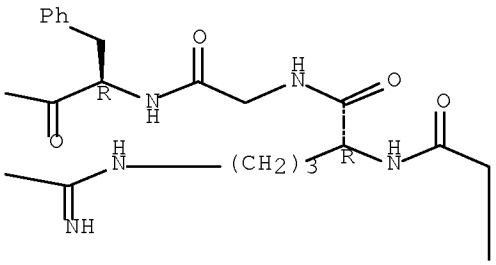
RN 956489-93-3 ZCAPLUS
CN D-Argininamide, N2-[2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-D-arginylglycyl-D-phenylalanyl-D-phenylalanyl-D-valyl-D-leucyl-D-lysylglycyl-D-arginyl-D-arginyl-D-arginyl-D-arginyl- (CA INDEX NAME)

Absolute stereochemistry.

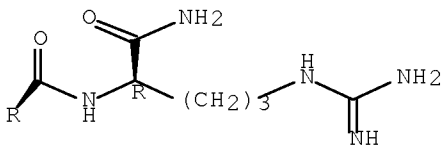
PAGE 1-A



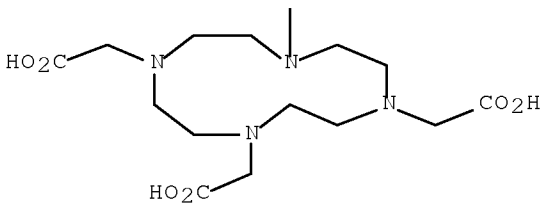
PAGE 1-B



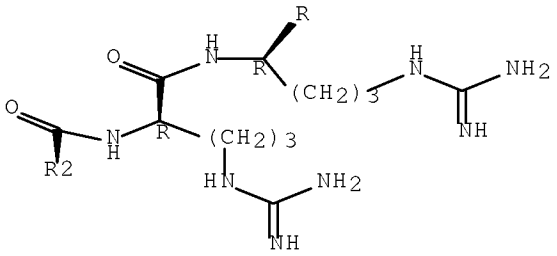
PAGE 2-A



PAGE 2-B



PAGE 3-A



L79 ANSWER 2 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:410019 ZCAPLUS Full-text
DOCUMENT NUMBER: 146:415599
TITLE: Neuropeptide Y analogs for treating and diagnosing Y1 receptor-expressing breast cancer
INVENTOR(S): Srinivasan, Ananth
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007039318	A2	20070412	WO 2006-EP9812	20061005
WO 2007039318	A3	20070705		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-723909P P 20051006

AB The neuropeptide Y(NPY)-receptor-subtype Y1 is expressed differentially from breast tumor cells and is therefore an advantageous target mol. for the mol. imaging of breast cancer. Peptide analogs were synthesized, whose sequence is reduced to the receptor-binding sections of the natural ligand NPY. These Y1 receptor-selective peptide analogs contain unnatural amino acids that increase the receptor affinity and are to ensure the stability of the greatly shortened peptide. New NPY analogs, which are to be used as radioligands, were tested for their binding affinity and selectivity for the Y1 receptor. To this end, in-vitro binding tests with Y1- or Y2 receptor-expressing cell lines were established and optimized. Then, the binding affinities of the NPY analogs were determined In this case, a peptide (P2489) was identified, whose highest binding affinity was determined with a Ki of 42.8 nmol of Y1 receptor-

expressing SK-N-MC cells and whose selectivity for the Y1 receptor could be detected by the fact that there is no binding to Y2 receptor-expressing MHH-NB-11 cells. As an addnl. NPY analog, peptide fW7 contained the unnatural amino acid β-aminocyclopropanecarboxylic acid on positions 32 and 34, by which the binding to the Y1 receptor was influenced in a pos. manner. A direct coupling of the chelating agent DOTA, which is necessary for the radiometal labeling of the peptides, to the N-terminal end of the peptides resulted in the loss of the binding affinity. By indirect coupling of the DOTA to the peptide fW7 via a spacer, this loss could be reduced, and fW7(DOTA) had a high binding affinity (Ki = 62.8 nmol) similar to P2489.

CC 2-10 (Mammalian Hormones)

IT 13981-56-1D, 18 F, complexes with neuropeptide Y analogs, biological studies 14133-76-7D, 99Tc, metastable, complexes with neuropeptide Y analogs, biological studies 14265-75-9D, complexes with neuropeptide Y analogs, biological studies 15750-15-9D, 111In, complexes with neuropeptide Y analogs, biological studies 15757-14-9D, complexes with neuropeptide Y analogs, biological studies 82785-45-3D, Neuropeptide Y, analogs 705283-66-5D, labeled 934183-14-9D, labeled 934183-15-0D, labeled 934183-16-1D, labeled 934350-78-4D, labeled 934350-82-0D, labeled 934350-86-4D, labeled 934350-87-5D, labeled
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(neuropeptide Y analogs for treating and diagnosing Y receptor-expressing breast cancer)

IT 705283-66-5 934183-14-9 934183-15-0 934183-16-1 934350-78-4 934350-82-0 934350-86-4 934350-87-5
RL: DGN (Diagnostic use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuropeptide Y analogs for treating and diagnosing Y receptor-expressing breast cancer)

IT 934183-16-1D, 177-Lu-DOTA complexes 934350-88-6
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)
(neuropeptide Y analogs for treating and diagnosing Y receptor-expressing breast cancer)

IT 14133-76-7D, 99Tc, metastable, complexes with neuropeptide Y analogs, biological studies 14265-75-9D, complexes with neuropeptide Y analogs, biological studies 15750-15-9D, 111In, complexes with neuropeptide Y analogs, biological studies 15757-14-9D, complexes with neuropeptide Y analogs, biological studies 934183-15-0D, labeled
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(neuropeptide Y analogs for treating and diagnosing Y receptor-expressing breast cancer)

RN 14133-76-7 ZCAPLUS

CN Technetium, isotope of mass 99 (CA INDEX NAME)

^{99}Tc

RN 14265-75-9 ZCAPLUS

CN Lutetium, isotope of mass 177 (CA INDEX NAME)

^{177}Lu

RN 15750-15-9 ZCAPLUS
CN Indium, isotope of mass 111 (CA INDEX NAME)

^{111}In

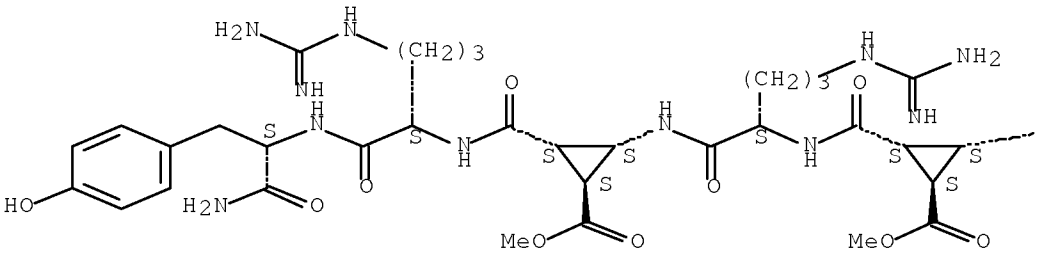
RN 15757-14-9 ZCAPLUS
CN Gallium, isotope of mass 68 (CA INDEX NAME)

^{68}Ga

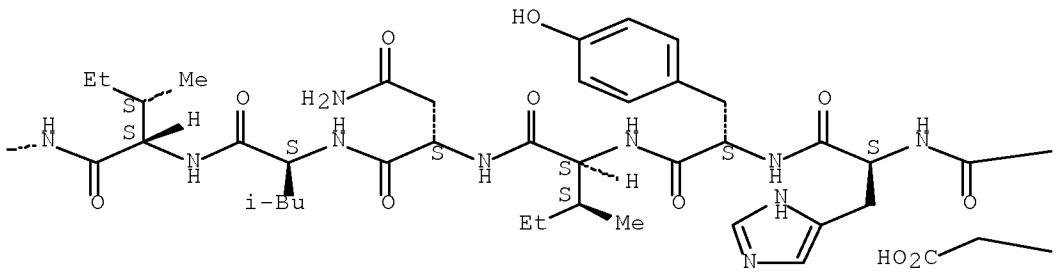
RN 934183-15-0 ZCAPLUS
CN L-Tyrosinamide, N2-[2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginyl-L-histidyl-L-tyrosyl-L-isoleucyl-L-asparaginyl-L-leucyl-L-isoleucyl-(1S,2S,3S)-2-amino-3-(methoxycarbonyl)cyclopropanecarbonyl-L-arginyl-(1S,2S,3S)-2-amino-3-(methoxycarbonyl)cyclopropanecarbonyl-L-arginyl- (CA INDEX NAME)

Absolute stereochemistry.

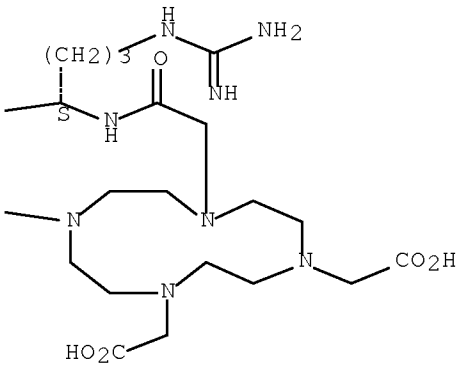
PAGE 1-A



PAGE 1-B



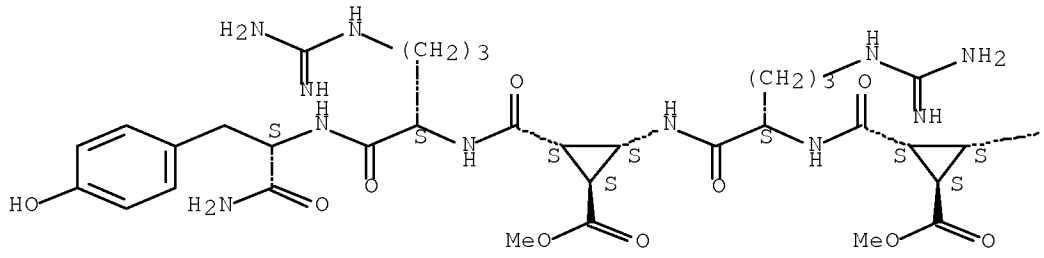
PAGE 1-C



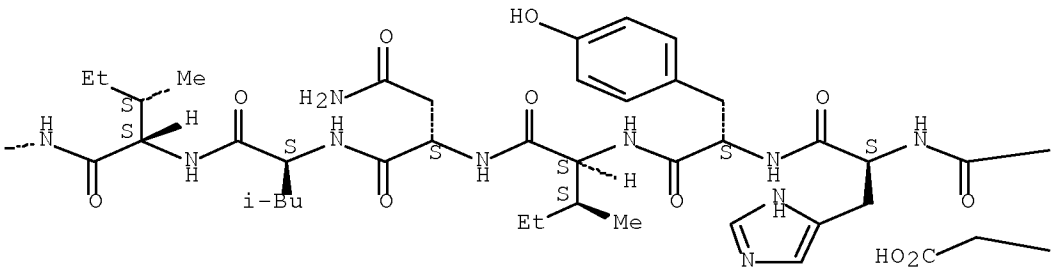
IT 934183-15-0
RL: DGN (Diagnostic use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuropeptide Y analogs for treating and diagnosing Y receptor-expressing breast cancer)
RN 934183-15-0 ZCAPLUS
CN L-Tyrosinamide, N2-[2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginyl-L-histidyl-L-tyrosyl-L-isoleucyl-L-asparaginyl-L-leucyl-L-isoleucyl-(1S,2S,3S)-2-amino-3-(methoxycarbonyl)cyclopropanecarbonyl-L-arginyl-(1S,2S,3S)-2-amino-3-(methoxycarbonyl)cyclopropanecarbonyl-L-arginyl- (CA INDEX NAME)

Absolute stereochemistry.

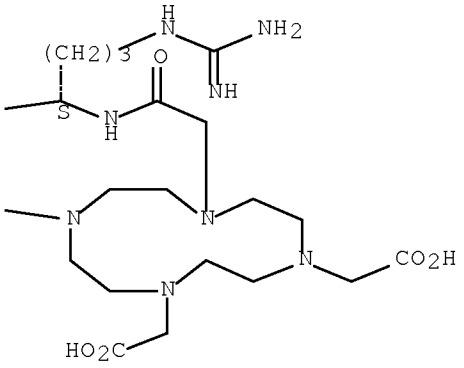
PAGE 1-A



PAGE 1-B



PAGE 1-C

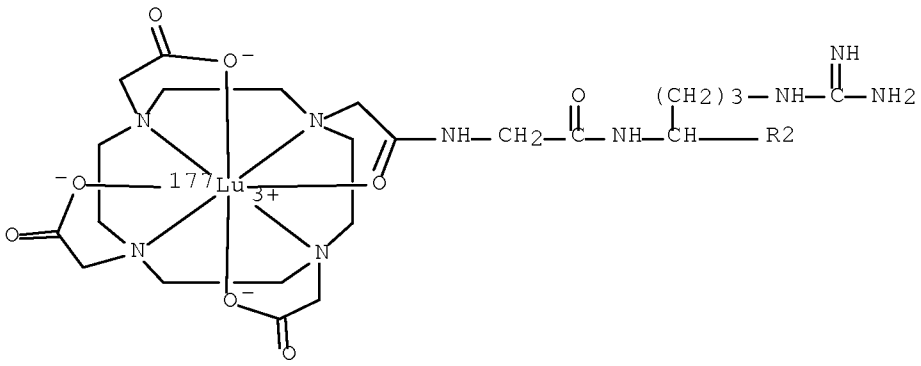


IT 934350-88-6
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)
(neuropeptide Y analogs for treating and diagnosing Y receptor-expressing breast cancer)

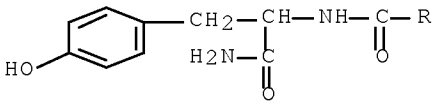
RN 934350-88-6 ZCAPLUS

CN Lutetium-177Lu, [N-[2-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]glycyl-L-arginyl-L-histidyl-L-tyrosyl-L-isoleucyl-L-asparaginyl-L-leucyl-L-isoleucyl-L-threonyl-L-arginyl-2-aminocyclohexanecarbonyl-L-arginyl-L-tyrosinamidato(3-)]- (CA INDEX NAME)

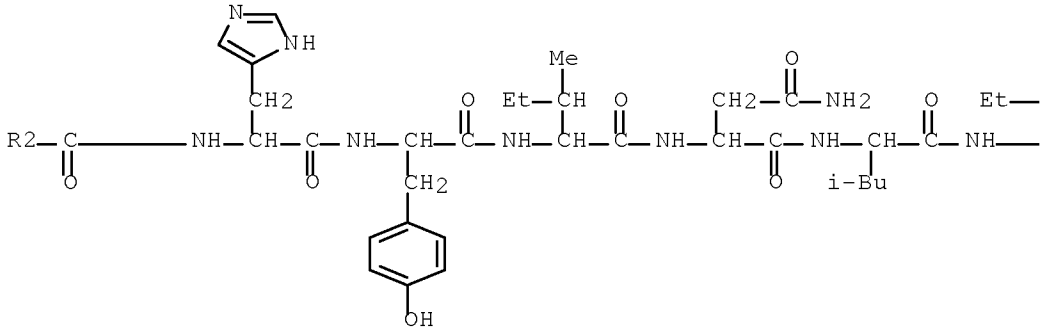
PAGE 1-A



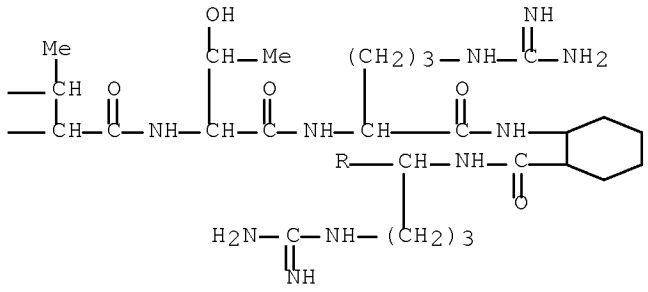
PAGE 2-A



PAGE 3-A



PAGE 3-B



L79 ANSWER 3 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1274397 ZCAPLUS Full-text
DOCUMENT NUMBER: 147:183765
TITLE: Evaluation of a new biotin-DOTA conjugate for pretargeted antibody-guided radioimmunotherapy (PAGRIT)
AUTHOR(S): Urbano, Nicoletta; Papi, Stefano; Ginanneschi, Mauro; Santis, Rita; Pace, Silvia; Lindstedt, Ragnar; Ferrari, Liliana; Choi, SunJu; Paganelli, Giovanni; Chinol, Marco
CORPORATE SOURCE: Division of Nuclear Medicine, European Institute of Oncology, Milan, 20141, Italy
SOURCE: European Journal of Nuclear Medicine and Molecular Imaging (2007), 34(1), 68-77
CODEN: EJNMA6; ISSN: 1619-7070
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose: A novel biotin-DOTA conjugate (r-BHD: reduced biotinamidohexylamine-DOTA) was investigated in order to provide an efficient pretargeted antibody-guided radioimmunotherapy (PAGRIT) application. Preclin. and clin. results are described. Methods: 90Y and 177Lu were used to label r-BHD. The effect of pH and a wide range of specific activities were studied. Radiolabeled r-BHD was tested for affinity towards avidin and for stability in saline or in human serum with and without ascorbic acid. Pharmacokinetic data were collected and organ biodistribution evaluated in a tumor-bearing pretargeted animal model. A pilot study was performed in a metastatic melanoma patient and dosimetry was estimated Results: High radiochem. purity (>99%) was routinely achieved with 90Y or 177Lu in sodium acetate buffer (1.0 M, pH 5.0) at a specific activity of 2.6 MBq/nmol. Both 90Y- and 177Lu-r-BHD were also prepared at higher specific activities. Radiolabeled r-BHD was stable up to 96 h in human serum and saline with the addition of ascorbic acid. The structural modifications proposed for the r-BHD stabilized it against enzymic degradation while retaining high binding affinity for avidin. Renal clearance appeared to be the main route of excretion in animals, and high tumor uptake was observed in the pretargeted animals. The patient study showed a total body clearance of .apprx.85% in 24 h, with a kidney absorbed dose of 1.5 mGy/MBq. Tumor uptake was rapid and the calculated dose to a 10-mm tumor lesion was .apprx.12 mGy/MBq. Conclusion: These results indicate that the new biotin-DOTA conjugate may be a suitable candidate for pretargeting trials.

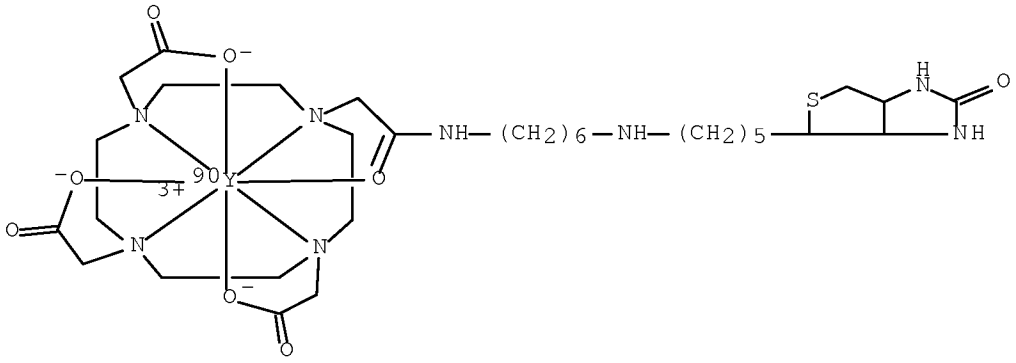
CC 8-9 (Radiation Biochemistry)
IT 58-85-5D, DOTA conjugates, Lu-177 complexes 14265-75-9D, 177Lu, complexes with DOTA-biotin, biological studies 60239-18-1D, DOTA, biotin

conjugates, Lu-177 complexes 586962-90-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of new biotin-DOTA conjugate for pretargeted antibody-guided radioimmunotherapy)

IT 586962-90-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of new biotin-DOTA conjugate for pretargeted antibody-guided radioimmunotherapy)

RN 586962-90-5 ZCAPLUS

CN Yttrium-90Y, [10-[2-[[6-[[5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)pentyl]amino]hexyl]amino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,.kappa.N10,κO1,κo4,κO7]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 4 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:734439 ZCAPLUS Full-text
DOCUMENT NUMBER: 145:195598
TITLE: Compounds having RD targeting motifs
INVENTOR(S): Achilefu, Samuel
PATENT ASSIGNEE(S): Washington University, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006078914	A1	20060727	WO 2006-US2056	20060120

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-645816P P 20050121

OTHER SOURCE(S): MARPAT 145:195598

AB The present invention provides compds. that have motifs that target the compds. to cells that express integrins. In particular, the compds. have peptides with one or more RD motifs conjugated to an agent selected from an imaging agent and a targeting agent. The compds. may be used to detect, monitor and treat a variety of disorders mediated by integrins.

CC 63-5 (Pharmaceuticals)

IT 91037-65-9D, conjugates with cypate and glucosamine 111119-28-9D, DTPA conjugates 111844-19-0D, conjugates with cypate and octreotate 317809-26-0, Cypate 317809-26-0D, Cypate, conjugates with peptides 901439-51-8D, DTPA conjugates 901442-07-7D, conjugates with cypate and glucosamine 901442-72-6 901442-80-6 901442-87-3 901442-94-2 901443-01-4 901443-47-8 901443-47-8D, conjugates with peptides 901443-61-6 901443-68-3 901443-74-1 901443-82-1 901443-89-8 901443-96-7 901444-04-0 901444-12-0 901444-20-0D, DTPA conjugates 901444-27-7D, DTPA conjugates 901444-34-6D, DTPA conjugates 901444-41-5D, DTPA conjugates 901444-63-1 901444-71-1 901444-79-9 901444-86-8 901445-34-9 901445-41-8 901445-48-5
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostic and therapeutic peptide conjugates targeted to integrin-pos. cells)

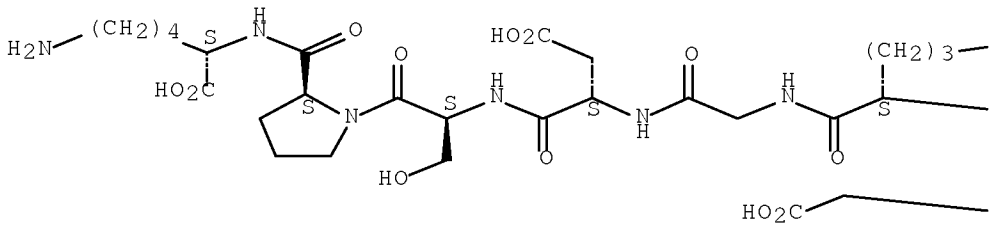
IT 901444-63-1 901444-71-1
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diagnostic and therapeutic peptide conjugates targeted to integrin-pos. cells)

RN 901444-63-1 ZCAPLUS

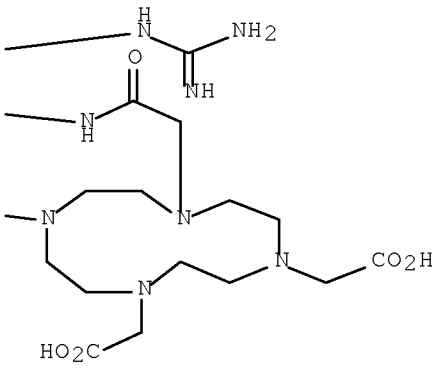
CN L-Lysine, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginylglycyl-L-α-aspartyl-L-seryl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



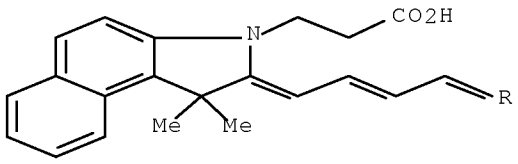
PAGE 1-B



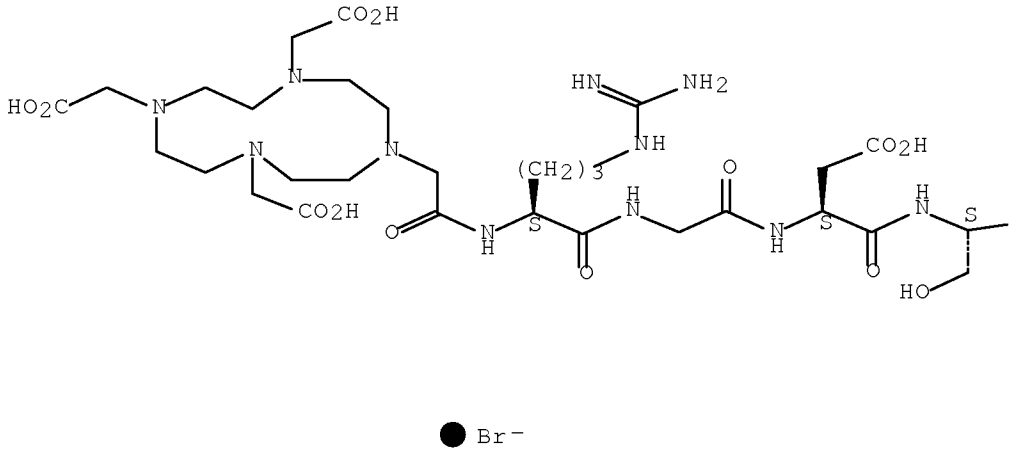
RN 901444-71-1 ZCAPLUS
CN L-Lysinamide, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginylglycyl-L-α-aspartyl-L-seryl-L-prolyl-N6-[3-[2-[7-[3-(2-carboxyethyl)-1,3-dihydro-1,1-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-1H-benz[e]indolio]-1-oxopropyl]-, bromide (9CI) (CA INDEX NAME)

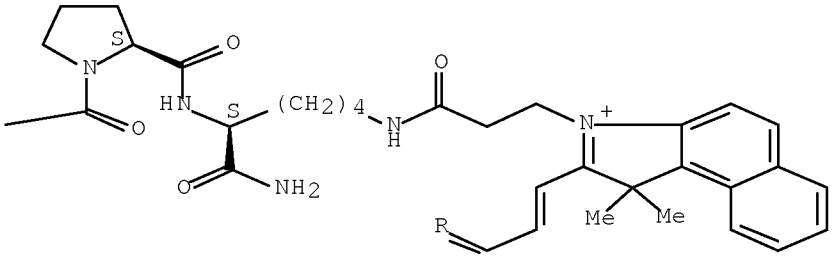
Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A



PAGE 2-A





REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 5 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:625378 ZCAPLUS Full-text
DOCUMENT NUMBER: 145:243952
TITLE: Magnetic resonance imaging of tumor cells by targeting the amino acid transport system
AUTHOR(S): Lattuada, Luciano; Demattio, Silvia; Vincenzi, Veronica; Cabella, Claudia; Visigalli, Massimo; Aime, Silvio; Crich, Simonetta Geninatti; Gianolio, Eliana
CORPORATE SOURCE: CRM Chemistry, Bracco Imaging SpA, Milan, 20134, Italy
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(15), 4111-4114
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:243952

AB An early diagnosis of cancer is crucial in the battle against this disease and the in vivo visualization of tumors at cellular level is still the most challenging goal. In order to target tumor cells, we took into account their increased metabolism and amino acid nutrients or pseudo-nutrients, which are actively transported through the cell membrane, have been chosen as vectors for new MRI contrast agents. For this reason new gadolinium complexes conjugated to agmatine, arginine, and glutamine have been synthesized and studied.

CC 8-9 (Radiation Biochemistry)
ST MRI tumor aminoacid transport prepn gadolinium complex conjugate; agmatine arginine glutamine conjugate gadolinium MRI contrast agent
IT Neoplasm
(MRI of tumor by targeting amino acid transport: preparation of gadolinium complexes conjugated to agmatine, arginine, and glutamine)
IT Imaging agents
(NMR contrast; MRI of tumor by targeting amino acid transport: preparation of gadolinium complexes conjugated to agmatine, arginine, and glutamine)
IT Imaging
(NMR; MRI of tumor by targeting amino acid transport: preparation

of gadolinium complexes conjugated to agmatine, arginine, and glutamine)

IT Imaging
(tumor; MRI of tumor by targeting amino acid transport: preparation of gadolinium complexes conjugated to agmatine, arginine, and glutamine)

IT 906078-01-1P 906078-02-2P 906078-03-3P 906078-04-4P 906078-05-5P 906078-06-6P 906078-07-7P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MRI of tumor by targeting amino acid transport: preparation of gadolinium complexes conjugated to agmatine, arginine, and glutamine)

IT 79-04-9, Chloroacetylchloride 6066-82-6, N-Hydroxysuccinimide 41444-88-6 115608-61-2 128009-23-4 174267-75-5 585531-74-4 805233-27-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(MRI of tumor by targeting amino acid transport: preparation of gadolinium complexes conjugated to agmatine, arginine, and glutamine)

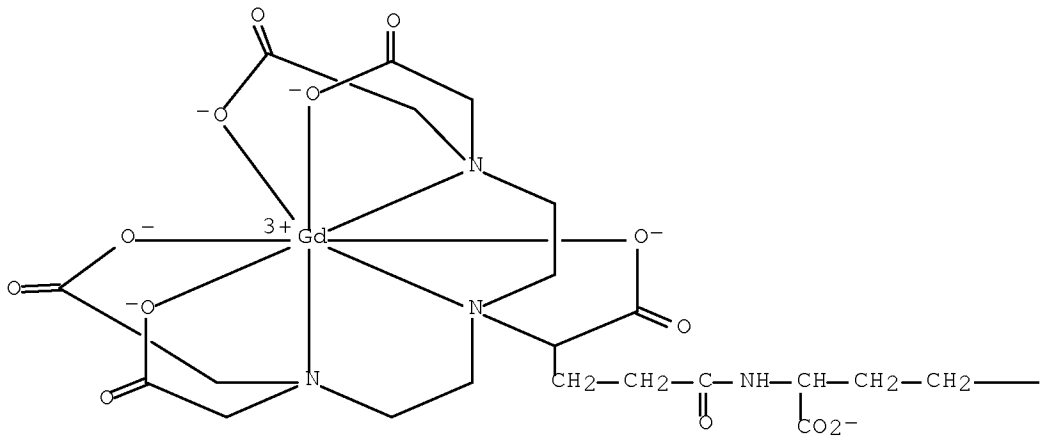
IT 905985-29-7P 905985-30-0P 905985-31-1P 905985-32-2P 905985-34-4P 905985-35-5P 905985-36-6P 905985-37-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(MRI of tumor by targeting amino acid transport: preparation of gadolinium complexes conjugated to agmatine, arginine, and glutamine)

IT 906078-01-1P 906078-02-2P 906078-03-3P 906078-04-4P 906078-05-5P 906078-06-6P 906078-07-7P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MRI of tumor by targeting amino acid transport: preparation of gadolinium complexes conjugated to agmatine, arginine, and glutamine)

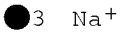
RN 906078-01-1 ZCAPLUS

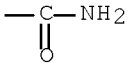
CN Gadolinate(3-), [N,N-bis[2-[bis[(carboxy-κO)methyl]amino-κN]ethyl]-L-γ-glutamyl-κN,κO1-L-glutaminato(6-)]-, trisodium (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

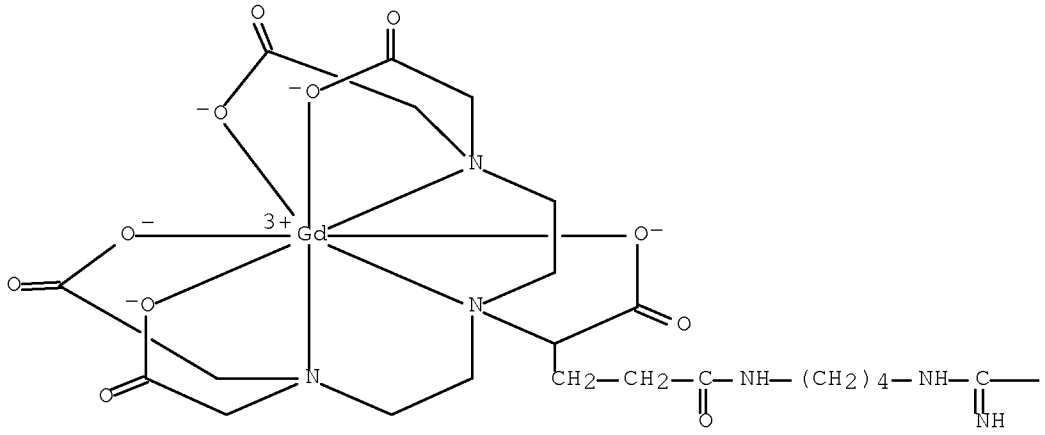




RN 906078-02-2 ZCAPLUS

CN Gadolinate(2-), [1-amino-12-[2-[bis[(carboxy-κO)methyl]amino-κN]ethyl]-11-(carboxy-κO)-15-[(carboxy-κO)methyl]-1-imino-8-oxo-2,7,12,15-tetraazaheptadecan-17-oato(5-)-κN12,κN15,κO17]-, disodium (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

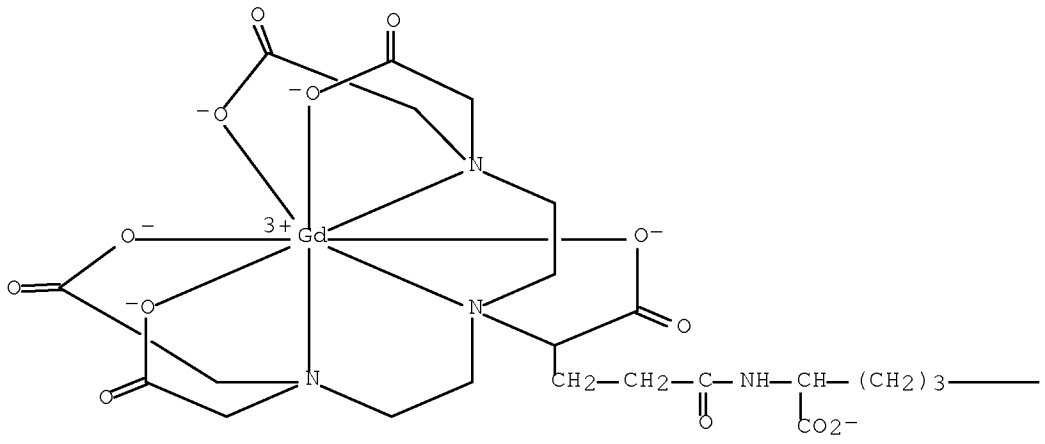
●2 Na^+

—NH_2

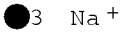
RN 906078-03-3 ZCAPLUS

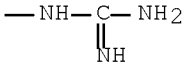
CN Gadolinate(3-), [N,N-bis[2-[bis[(carboxy-κO)methyl]amino-κN]ethyl]-L-γ-glutamyl-κN,κO1-L-argininato(6-)]-, trisodium (9CI) (CA INDEX NAME)

PAGE 1-A



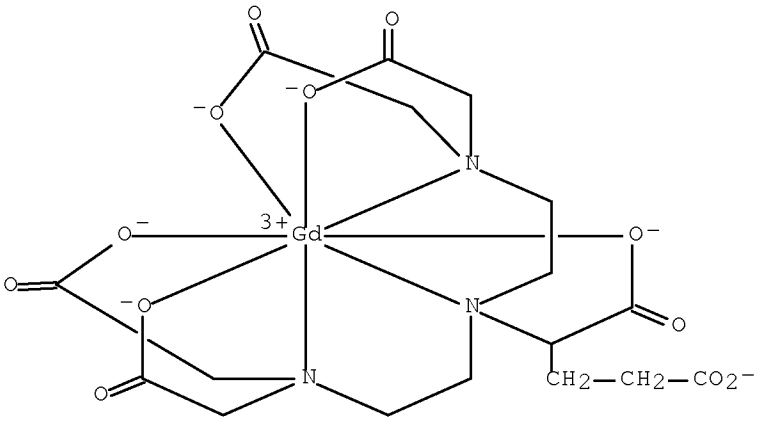
PAGE 1-B



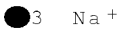


RN 906078-04-4 ZCAPLUS
CN Gadolinate(3-), [N,N-bis[2-[bis[(carboxy-κO)methyl]amino-κN]ethyl]-L-glutamato(6-)-κN2,κO1]-, trisodium (9CI) (CA INDEX NAME)

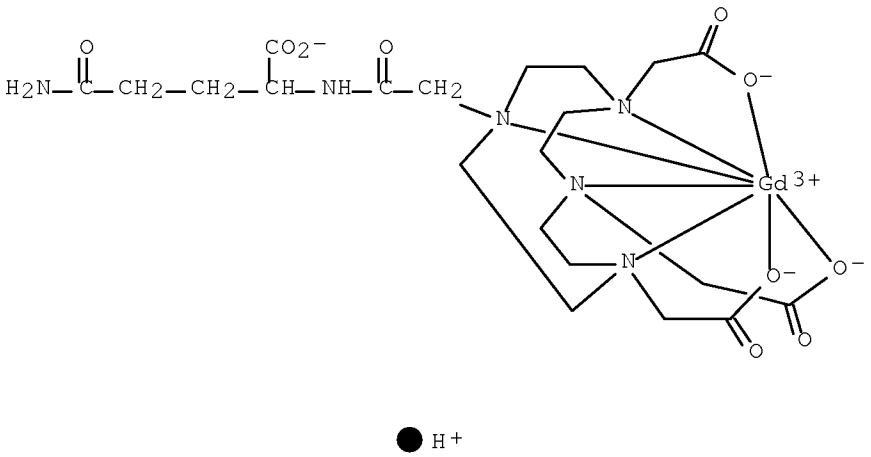
PAGE 1-A



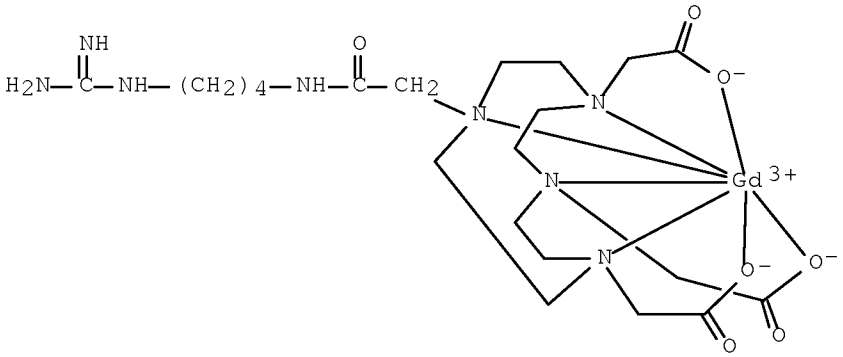
PAGE 2-A



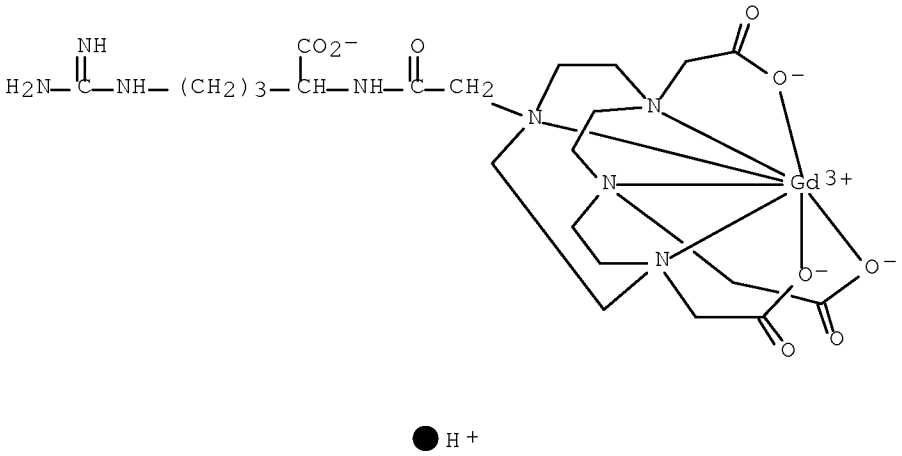
RN 906078-05-5 ZCAPLUS
CN Gadolinate(1-), [10-[2-[(4-amino-1-carboxy-4-oxobutyl)amino]-2-oxoethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(4-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-, hydrogen (9CI) (CA INDEX NAME)



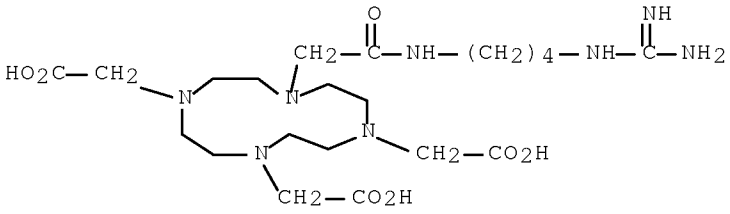
RN 906078-06-6 ZCAPLUS
CN Gadolinium, [10-[2-[[4-[(aminoiminomethyl)amino]butyl]amino]-2-oxoethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(7-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-(9CI) (CA INDEX NAME)



RN 906078-07-7 ZCAPLUS
CN Gadolinate(1-), [10-[2-[[4-[(aminoiminomethyl)amino]-1-carboxybutyl]amino]-2-oxoethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(4-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-, hydrogen (9CI) (CA INDEX NAME)

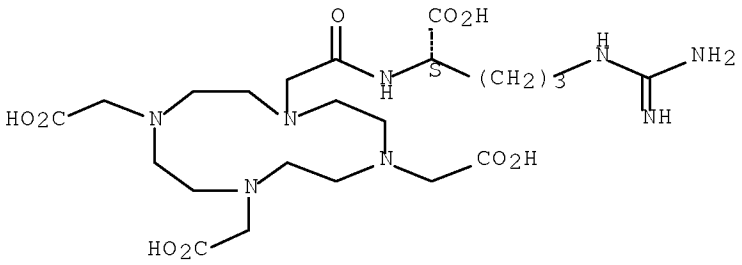


IT 905985-35-5P 905985-37-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(MRI of tumor by targeting amino acid transport: preparation of gadolinium complexes conjugated to agmatine, arginine, and glutamine)
RN 905985-35-5 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[4-[(aminoiminomethyl)amino]butyl]amino]-2-oxoethyl]- (CA INDEX NAME)



RN 905985-37-7 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(1S)-4-[(aminoiminomethyl)amino]-1-carboxybutyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



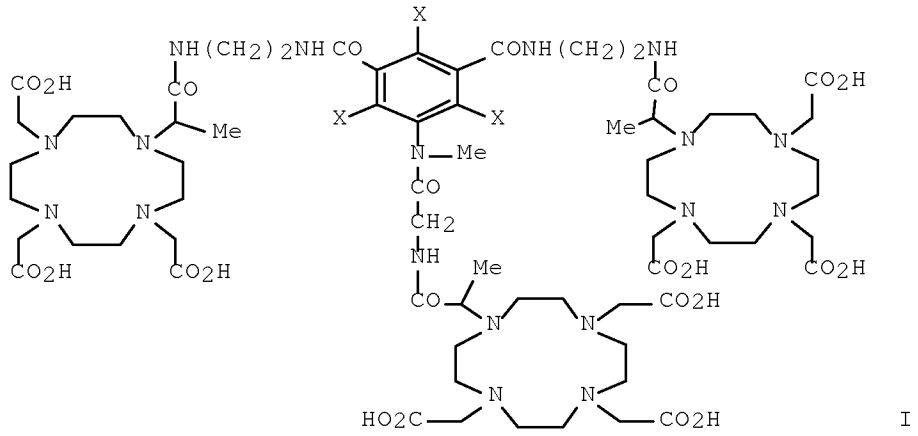
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 6 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1289862 ZCAPLUS Full-text
DOCUMENT NUMBER: 144:31701
TITLE: Preparation of metal complexes of trimeric DOTA-macrocyclic substituted aminoisophthalate trihalophenyl derivatives
INVENTOR(S): Harto, Juan R.; Martin, Jose L.; Platzek, Johannes; Schirmer, Heiko; Weinmann, Hanns-Joachim; Carretero, Jose
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005115997	A1	20051208	WO 2005-EP4493	20050422
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004026103	A1	20051222	DE 2004-102004026103	20040525
EP 1748992	A1	20070207	EP 2005-741025	20050422
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2008500293	T	20080110	JP 2007-513721	20050422
US 2006120965	A1	20060608	US 2005-274895	20051116

PRIORITY APPLN. INFO.:
DE 2004-102004026103A 20040525
US 2004-575417P P 20040601
WO 2005-EP4493 W 20050422
US 2005-135656 A1 20050524

OTHER SOURCE(S): MARPAT 144:31701
GI



I

AB The preparation is described for metal complexes of trihalobenzene functionalized with three DOTA-like chelating groups (I), where X = bromo or iodo. These complexes are suitable as contrast agents. Thus, the ligand I (X = iodo) was prepared in a multistep procedure and was used to prepare Gd, Dy, Yb and Y complexes.

IC ICM C07D257-02
ICS A61K049-04; A61K051-04; A61K049-08; C07K005-023; C07K005-02

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 8, 28

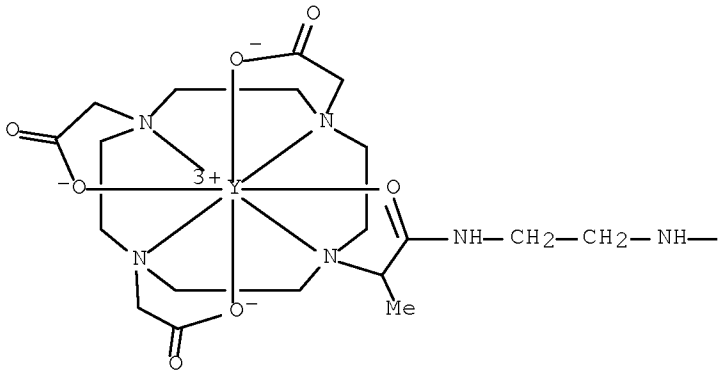
IT 7429-91-6P, Dysprosium, preparation 7439-89-6P, Iron, preparation 7439-96-5P, Manganese, preparation 7440-53-1P, Europium, preparation 7440-54-2P, Gadolinium, preparation 870475-42-6P 870475-43-7P 870475-44-8P 870475-45-9P 870475-48-2DP, metal complexes
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of metal complexes with trihalobenzene functionalized with three DOTA-like chelating groups for use as contrast agents)

IT 870475-45-9P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of metal complexes with trihalobenzene functionalized with three DOTA-like chelating groups for use as contrast agents)

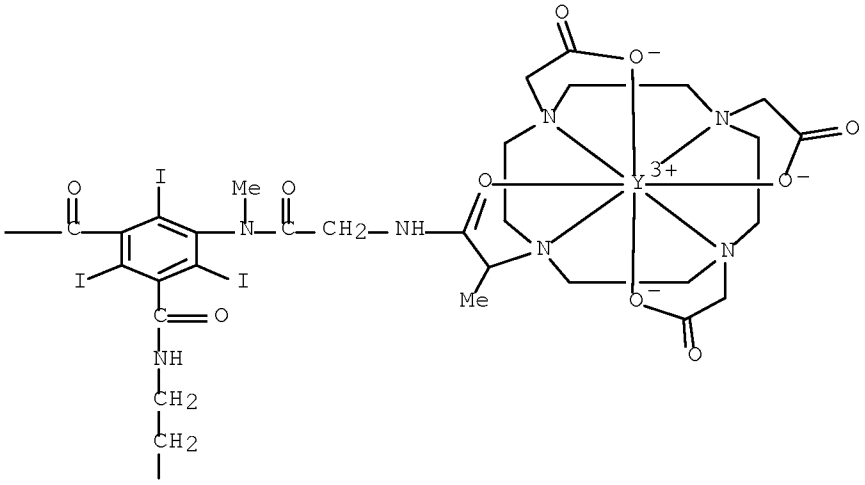
RN 870475-45-9 ZCAPLUS

CN Yttrium, [μ3-[[10,10'-[[2,4,6-triiodo-5-[methyl[[[1-(oxo-κO)-2-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]propyl]amino]acetyl]amino]-1,3-phenylene]bis[carbonylimino-2,1-ethanediylimino[1-methyl-2-(oxo-κO)-2,1-ethanediyl]]]bis[1,4,7,10-tetraazacyclododecane-1,4,7-triacetato-κN1,κN4,κN7,κN10,κO1,κO4,κO7]](9-)]]tri- (9CI) (CA INDEX NAME)

PAGE 1-A

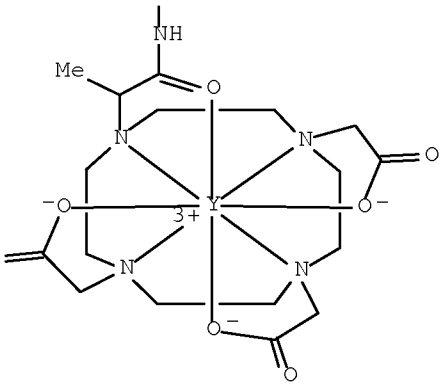


PAGE 1-B



PAGE 2-A

PAGE 2-B



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 7 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1220695 ZCAPLUS Full-text
DOCUMENT NUMBER: 143:471966
TITLE: Macrocycle-substituted trimer halogen-benzene derivatives
INVENTOR(S): Harto, Juan R.; Martin, Jose L.; Platzek, Johannes; Schirmer, Heiko; Weinmann, Hanns-Joachim; Carretero, Jose
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005108379	A1	20051117	WO 2005-EP4319	20050419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004023093	B3	20060302	DE 2004-102004023093	20040505
EP 1742926	A1	20070117	EP 2005-742880	20050419
EP 1742926	B1	20070808		
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
AT 369347	T	20070815	AT 2005-742880	20050419
JP 2007536295	T	20071213	JP 2007-511925	20050419
ES 2289711	T3	20080201	ES 2005-742880	20050419

US 2006154989 A1 20060713 US 2005-272008 20051114
PRIORITY APPLN. INFO.: DE 2004-102004023093A 20040505
US 2004-574713P P 20040527
WO 2005-EP4319 W 20050419
US 2005-122248 A1 20050505
OTHER SOURCE(S): MARPAT 143:471966
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to rare earth, Fe and Mn complexes of I (X = Br or I' A1 = CONR1(CH2)nNR2(COCHZ1NH)mCOCHZ2K, A2 = NR1COCHZ2K (R1 and R1 = H, C1-2 alkyl group of monohydroxy C1-2 alkyl group; Z1 and Z2 = H or Me; n = 2-4; m = 0-1; K = 1,4,7,11-tetraazacyclotetradecane-1,4,7-triacetic acid group)) and said complexes are suitable as contrast agents. For example, II (H3L) was prepared in a multi step process starting from 2,4,6-triiodo-5-(methylamino)isophthaloyl dichloride and ethylenediamine, with subsequent reaction with 2-bromopropanoyl bromide, 1,4,7-tris(benzylcarbonyl)-1,4,7,11-tetraazacyclotetradecane with deprotection and reaction with chloroacetic acid. GdL in 58 % yield was prepared from II and Gd2O3.

IC ICM C07D257-02
ICS A61K051-04; A61K049-08

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 9, 28, 77

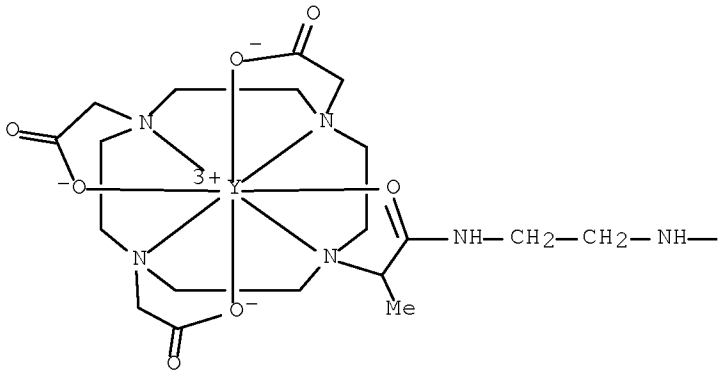
IT 7429-91-6DP, Dysprosium, complexes with tetraazacyclotetradecanetriacetic acid, isophthalic acid amide derivs. 7439-89-6DP, Iron, complexes with tetraazacyclotetradecanetriacetic acid, isophthalic acid amide derivs. 7439-96-5DP, Manganese, complexes with tetraazacyclotetradecanetriacetic acid, isophthalic acid amide derivs. 7440-53-1DP, Europium, complexes with tetraazacyclotetradecanetriacetic acid, isophthalic acid amide derivs. 7440-54-2DP, Gadolinium, complexes with tetraazacyclotetradecanetriacetic acid, isophthalic acid amide derivs. 869339-24-2P 869339-25-3P 869339-26-4P 869339-28-6P 869339-51-5DP, isophthalic acid amide derivs., transition metal complexes
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation as contrast agents)

IT 869339-26-4P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation as contrast agents)

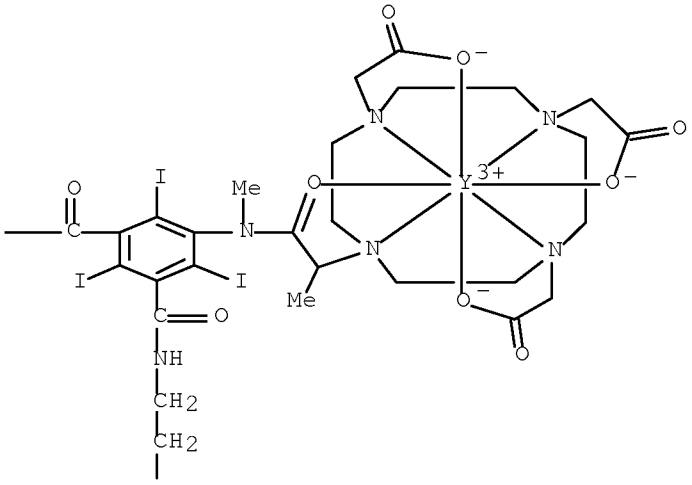
RN 869339-26-4 ZCAPLUS

CN Yttrium, [μ3-[[10,10'-[[2,4,6-triiodo-5-[methyl[1-(oxo-κO)-2-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]propyl]amino]-1,3-phenylene]bis[carbonylimino-2,1-ethanediylimino[1-methyl-2-(oxo-κO)-2,1-ethanediyl]]]bis[1,4,7,10-tetraazacyclododecane-1,4,7-triacetato-κN1,κN4,κN7,κN10,κO1,κO4,κO7]](9-)]]tri- (9CI) (CA INDEX NAME)

PAGE 1-A

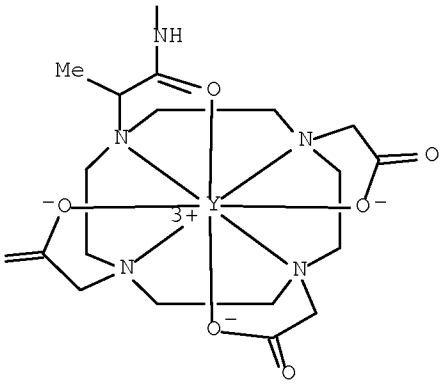


PAGE 1-B



PAGE 2-A

PAGE 2-B



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 8 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:799481 ZCAPLUS Full-text
DOCUMENT NUMBER: 141:320007
TITLE: Radiopharmaceuticals for cancer diagnosis and treatment
INVENTOR(S): Merlo, Adrian; Maecke, Helmut; Reubi, Jean-Claude; Good, Stephan
PATENT ASSIGNEE(S): Kantonsspital Basel, Switz.; Universitaet Bern
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004082722	A2	20040930	WO 2004-EP50329	20040318
WO 2004082722	A3	20050106		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1459769	A1	20040922	EP 2003-6061	20030319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004222531	A1	20040930	AU 2004-222531	20040318
CA 2519315	A1	20040930	CA 2004-2519315	20040318
EP 1603598	A2	20051214	EP 2004-721547	20040318
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				

JP 2007527366 T 20070927 JP 2006-505475 20040318
US 2007053837 A1 20070308 US 2005-549665 20050919
PRIORITY APPLN. INFO.: EP 2003-6061 A 20030319
WO 2004-EP50329 W 20040318
OTHER SOURCE(S): MARPAT 141:320007
AB The invention relates to radiopharmaceutical carriers consisting of a radiolabeled substance P analog conjugated to a chelating agent such as DOTAGA, DOTASA or DOTA, which are useful for targeting and treatment of brain tumors, especially gliomas.
IC ICM A61K051-00
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 8
IT 10098-91-6D, Yttrium 90, substance P-conjugated complexes, biological studies 13967-64-1D, Dysprosium 165, substance P-conjugated complexes, biological studies 13967-65-2D, Holmium 166, substance P-conjugated complexes, biological studies 13981-25-4D, Copper 64, substance P-conjugated complexes, biological studies 14119-08-5D, Gallium 66, substance P-conjugated complexes, biological studies 14119-09-6D, Gallium 67, substance P-conjugated complexes, biological studies 14191-64-1D, Praseodymium 142, substance P-conjugated complexes, biological studies 14265-75-9D, Lutetium 177, substance P-conjugated complexes, biological studies 14265-85-1D, Actinium 225, substance P-conjugated complexes, biological studies 14687-25-3D, Lead 203, substance P-conjugated complexes, biological studies 14809-53-1D, Yttrium 86, substance P-conjugated complexes, biological studies 14834-85-6D, Dysprosium 162, substance P-conjugated complexes, biological studies 14885-78-0D, Indium 113, substance P-conjugated complexes, biological studies 14913-49-6D, Bismuth 212, substance P-conjugated complexes, biological studies 14981-79-4D, Praseodymium 143, substance P-conjugated complexes, biological studies 15065-93-7D, Terbium 149, substance P-conjugated complexes, biological studies 15750-15-9D, Indium 111, substance P-conjugated complexes, biological studies 15757-14-9D, Gallium 68, substance P-conjugated complexes, biological studies 15757-86-5D, Copper 67, substance P-conjugated complexes, biological studies 15765-31-8D, Promethium 149, substance P-conjugated complexes, biological studies 15776-20-2D, Bismuth 213, substance P-conjugated complexes, biological studies 33507-63-0D, Substance P, conjugates of radionuclide complexes 36849-05-5D, Dysprosium 167, substance P-conjugated complexes, biological studies 77128-75-7D, conjugates of radionuclide complexes 110880-55-2D, conjugates of radionuclide complexes 110880-57-4D, conjugates of radionuclide complexes 766529-14-0D, conjugates of radionuclide complexes 766529-15-1D, conjugates of radionuclide complexes 766529-16-2D, conjugates of radionuclide complexes 766529-18-4D, conjugates of radionuclide complexes 766529-19-5D, conjugates of radionuclide complexes 766529-20-8D, conjugates of radionuclide complexes 766529-22-0D, conjugates of radionuclide complexes 766529-24-2D, conjugates of radionuclide complexes 766529-25-3D, conjugates of radionuclide complexes 766529-28-6D, conjugates of radionuclide complexes 766529-29-7D, conjugates of radionuclide complexes
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radiolabeled substance P conjugates for cancer diagnosis and treatment)
IT 767340-53-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(radiolabeled substance P conjugates for cancer diagnosis and treatment)

IT 766529-30-0P 766529-31-1P 766529-32-2P
766529-33-3P 766529-34-4P 766529-35-5P
766529-36-6P 766529-37-7P 766529-38-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radiolabeled substance P conjugates for cancer diagnosis and treatment)

IT 767340-54-5P 767340-55-6P 767340-56-7P
767340-57-8P 767340-58-9P 767340-59-0P
767340-60-3P 767340-61-4P 767340-62-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(radiolabeled substance P conjugates for cancer diagnosis and treatment)

IT 10098-91-6D, Yttrium 90, substance P-conjugated complexes, biological studies 13967-64-1D, Dysprosium 165, substance P-conjugated complexes, biological studies 13967-65-2D, Holmium 166, substance P-conjugated complexes, biological studies 13981-25-4D, Copper 64, substance P-conjugated complexes, biological studies 14119-08-5D, Gallium 66, substance P-conjugated complexes, biological studies 14119-09-6D, Gallium 67, substance P-conjugated complexes, biological studies 14191-64-1D, Praseodymium 142, substance P-conjugated complexes, biological studies 14265-75-9D, Lutetium 177, substance P-conjugated complexes, biological studies 14265-85-1D, Actinium 225, substance P-conjugated complexes, biological studies 14687-25-3D, Lead 203, substance P-conjugated complexes, biological studies 14809-53-1D, Yttrium 86, substance P-conjugated complexes, biological studies 14834-85-6D, Dysprosium 162, substance P-conjugated complexes, biological studies 14885-78-0D, Indium 113, substance P-conjugated complexes, biological studies 14913-49-6D, Bismuth 212, substance P-conjugated complexes, biological studies 14981-79-4D, Praseodymium 143, substance P-conjugated complexes, biological studies 15065-93-7D, Terbium 149, substance P-conjugated complexes, biological studies 15750-15-9D, Indium 111, substance P-conjugated complexes, biological studies 15757-14-9D, Gallium 68, substance P-conjugated complexes, biological studies 15757-86-5D, Copper 67, substance P-conjugated complexes, biological studies 15765-31-8D, Promethium 149, substance P-conjugated complexes, biological studies 15776-20-2D, Bismuth 213, substance P-conjugated complexes, biological studies 36849-05-5D, Dysprosium 167, substance P-conjugated complexes, biological studies
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radiolabeled substance P conjugates for cancer diagnosis and treatment)

RN 10098-91-6 ZCAPLUS
CN Yttrium, isotope of mass 90 (CA INDEX NAME)

^{90}Y

RN 13967-64-1 ZCAPLUS
CN Dysprosium, isotope of mass 165 (CA INDEX NAME)

^{165}Dy

RN 13967-65-2 ZCAPLUS
CN Holmium, isotope of mass 166 (CA INDEX NAME)

^{166}Ho

RN 13981-25-4 ZCAPLUS
CN Copper, isotope of mass 64 (CA INDEX NAME)

^{64}Cu

RN 14119-08-5 ZCAPLUS
CN Gallium, isotope of mass 66 (CA INDEX NAME)

^{66}Ga

RN 14119-09-6 ZCAPLUS
CN Gallium, isotope of mass 67 (CA INDEX NAME)

^{67}Ga

RN 14191-64-1 ZCAPLUS
CN Praseodymium, isotope of mass 142 (CA INDEX NAME)

^{142}Pr

RN 14265-75-9 ZCAPLUS
CN Lutetium, isotope of mass 177 (CA INDEX NAME)

^{177}Lu

RN 14265-85-1 ZCAPLUS
CN Actinium, isotope of mass 225 (CA INDEX NAME)

^{225}Ac

RN 14687-25-3 ZCAPLUS
CN Lead, isotope of mass 203 (CA INDEX NAME)

^{203}Pb

RN 14809-53-1 ZCAPLUS
CN Yttrium, isotope of mass 86 (CA INDEX NAME)

^{86}Y

RN 14834-85-6 ZCAPLUS
CN Dysprosium, isotope of mass 162 (CA INDEX NAME)

^{162}Dy

RN 14885-78-0 ZCAPLUS
CN Indium, isotope of mass 113 (CA INDEX NAME)

^{113}In

RN 14913-49-6 ZCAPLUS
CN Bismuth, isotope of mass 212 (CA INDEX NAME)

^{212}Bi

RN 14981-79-4 ZCAPLUS
CN Praseodymium, isotope of mass 143 (CA INDEX NAME)

^{143}Pr

RN 15065-93-7 ZCAPLUS
CN Terbium, isotope of mass 149 (CA INDEX NAME)

^{149}Tb

RN 15750-15-9 ZCAPLUS
CN Indium, isotope of mass 111 (CA INDEX NAME)

^{111}In

RN 15757-14-9 ZCAPLUS
CN Gallium, isotope of mass 68 (CA INDEX NAME)

^{68}Ga

RN 15757-86-5 ZCAPLUS
CN Copper, isotope of mass 67 (CA INDEX NAME)

^{67}Cu

RN 15765-31-8 ZCAPLUS
CN Promethium, isotope of mass 149 (CA INDEX NAME)

^{149}Pm

RN 15776-20-2 ZCAPLUS
CN Bismuth, isotope of mass 213 (CA INDEX NAME)

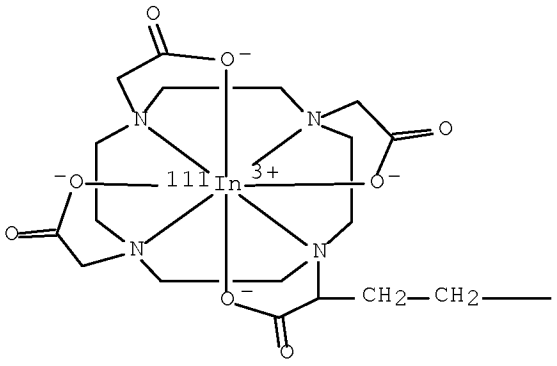
^{213}Bi

RN 36849-05-5 ZCAPLUS
CN Dysprosium, isotope of mass 167 (CA INDEX NAME)

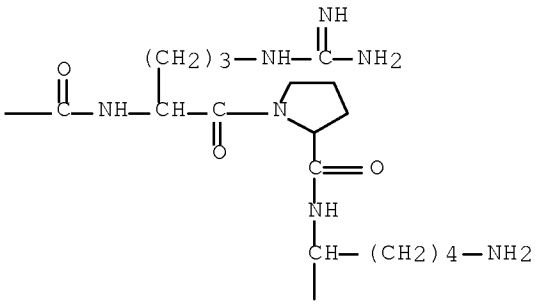
^{167}Dy

IT 767340-53-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(radiolabeled substance P conjugates for cancer diagnosis and treatment)
RN 767340-53-4 ZCAPLUS
CN Indate(1-)-111In, [N2-[4-(carboxy-κO)-1-oxo-4-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]butyl]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-L-phenylalanylglycyl-L-leucyl-L-methioninamidato(4-)]- (9CI) (CA INDEX NAME)

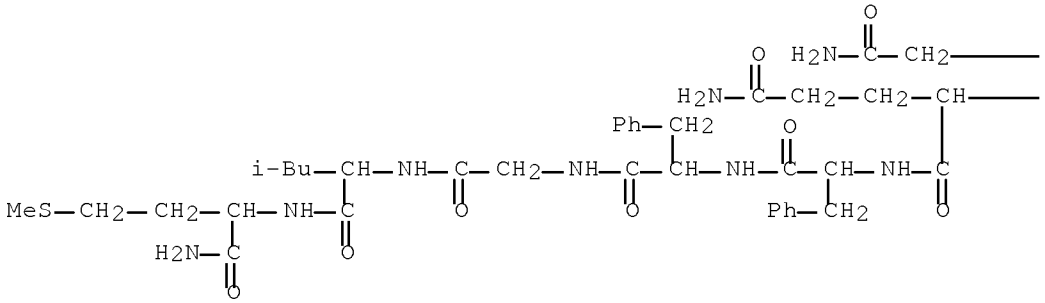
PAGE 1-A



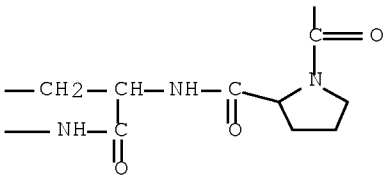
PAGE 1-B



PAGE 2-A



PAGE 2-B



IT 766529-31-1P 766529-32-2P 766529-33-3P
766529-34-4P 766529-35-5P 766529-36-6P
766529-37-7P 766529-38-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radiolabeled substance P conjugates for cancer diagnosis and

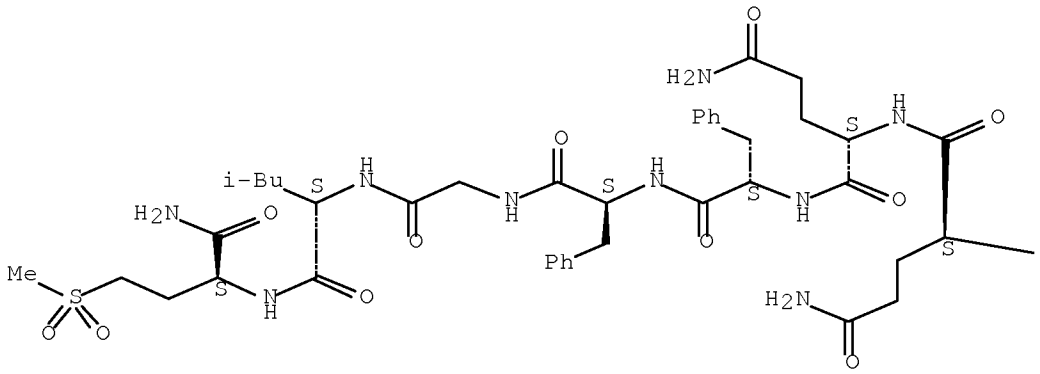
treatment)

RN 766529-31-1 ZCAPLUS

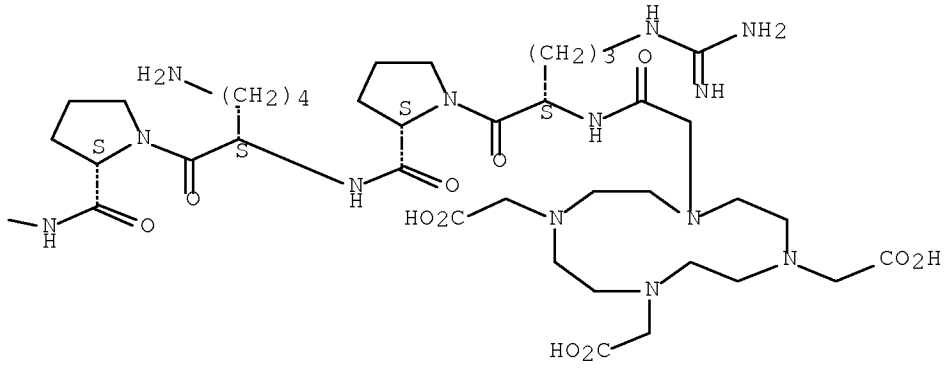
CN Substance P, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-11-[(2S)-2-amino-4-(methylsulfonyl)butanamide]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

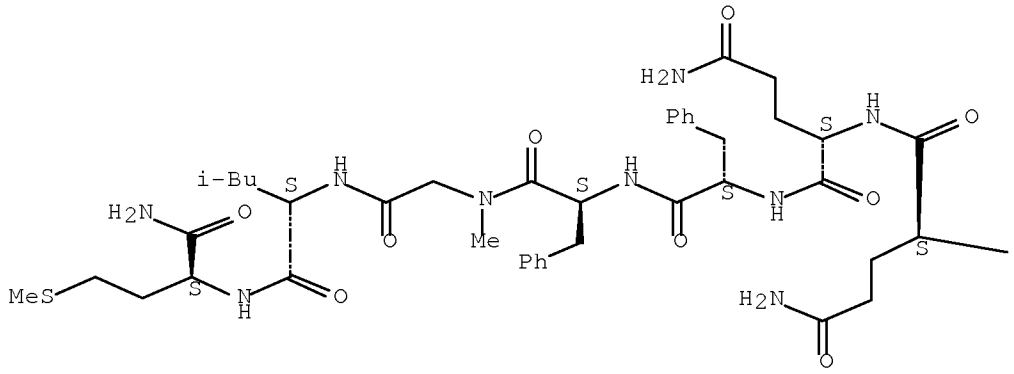


RN 766529-32-2 ZCAPLUS

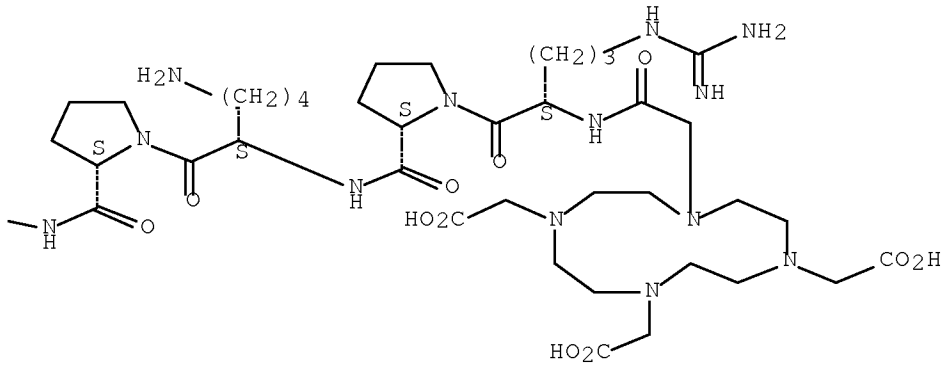
CN L-Methioninamide, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-L-phenylalanyl-N-methylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



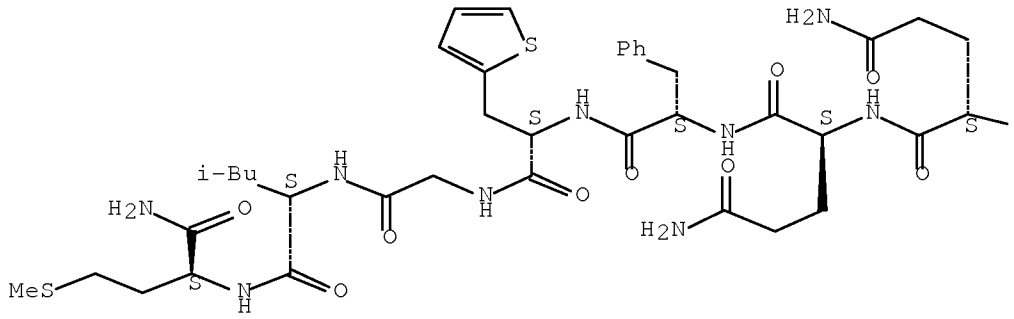
PAGE 1-B



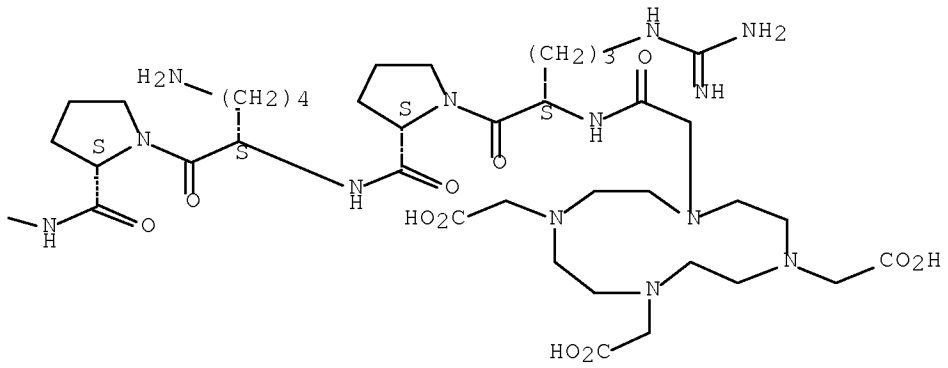
RN 766529-33-3 ZCAPLUS
CN L-Methioninamide, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-3-(2-thienyl)-L-alanylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



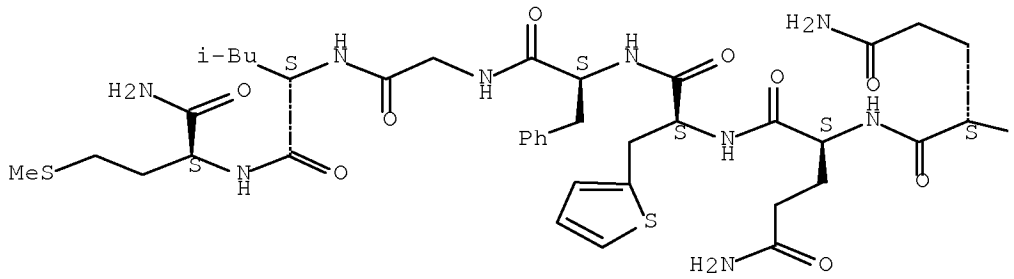
PAGE 1-B



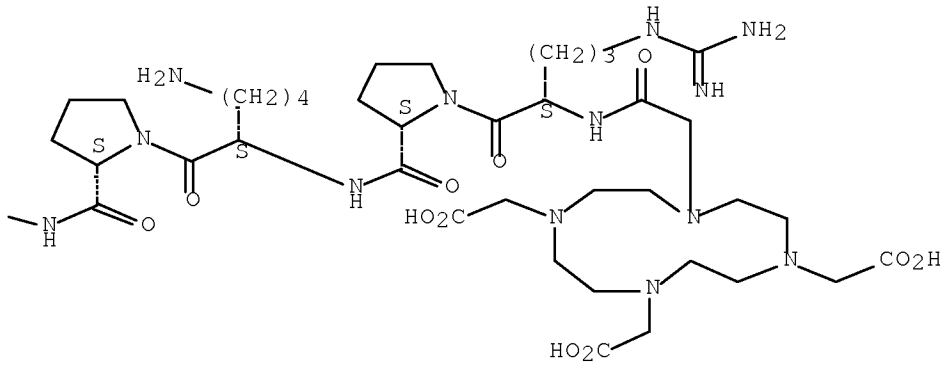
RN 766529-34-4 ZCAPLUS
CN L-Methioninamide, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-3-(2-thienyl)-L-alanyl-L-phenylalanylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



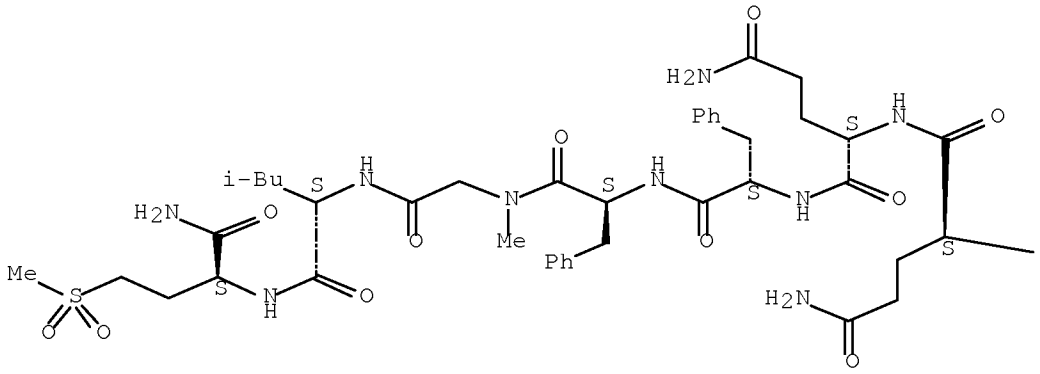
PAGE 1-B



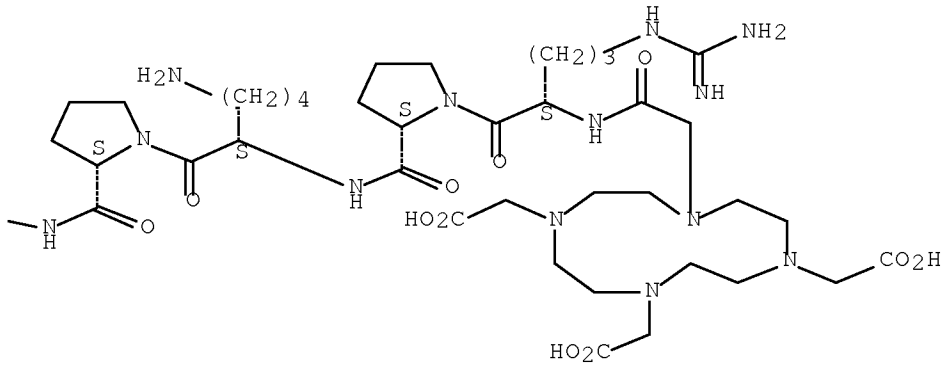
RN 766529-35-5 ZCAPLUS
CN Substance P, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-9-(N-methylglycine)-11-[(2S)-2-amino-4-(methylsulfonyl)butanamide]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

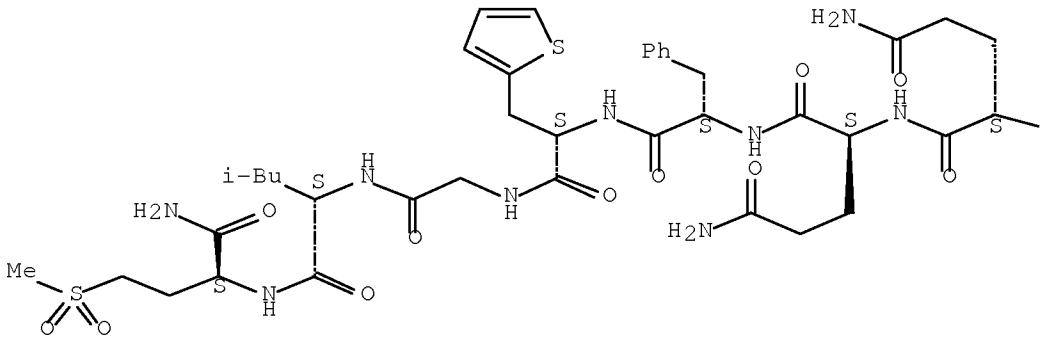


RN 766529-36-6 ZCAPLUS

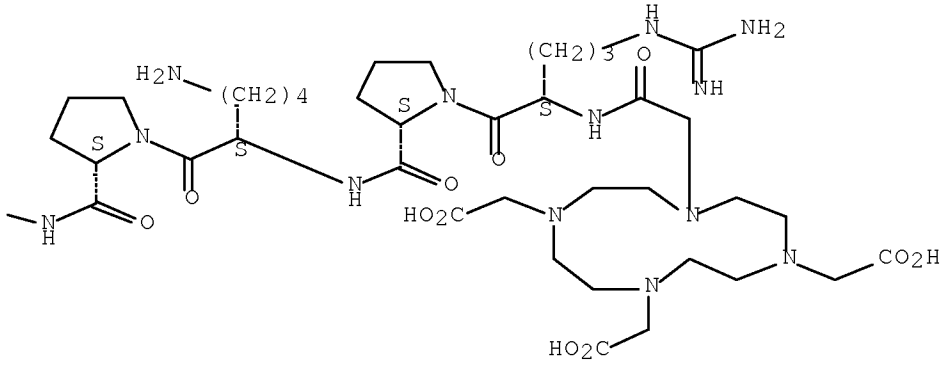
CN Butanamide, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-3-(2-thienyl)-L-alanylglycyl-L-leucyl-2-amino-4-(methylsulfonyl)-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



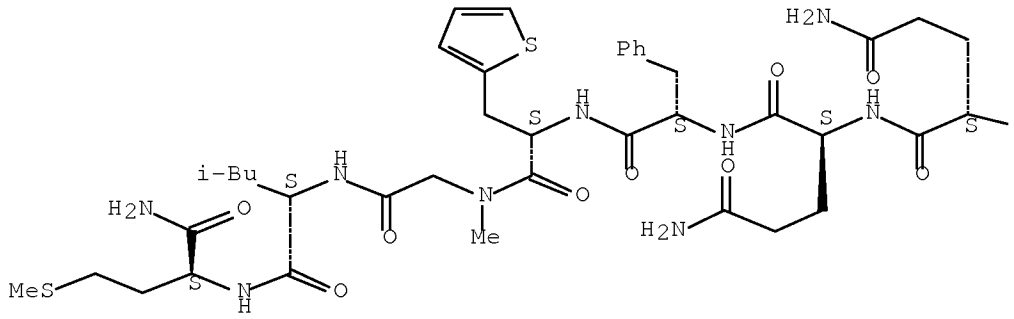
PAGE 1-B



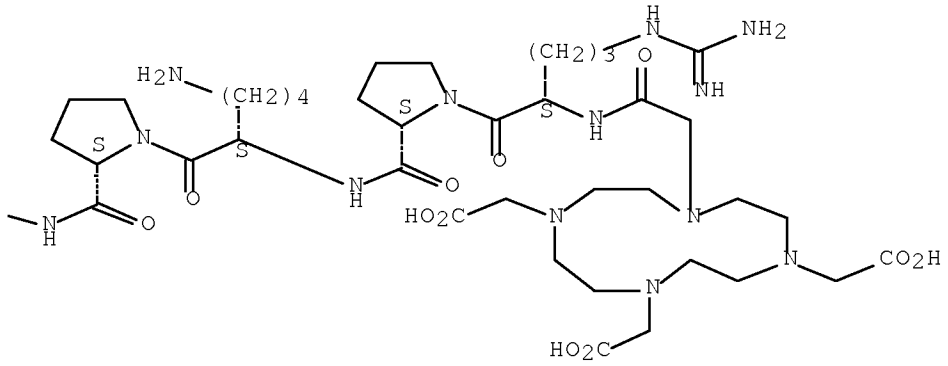
RN 766529-37-7 ZCAPLUS
CN L-Methioninamide, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-3-(2-thienyl)-L-alanyl-N-methylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



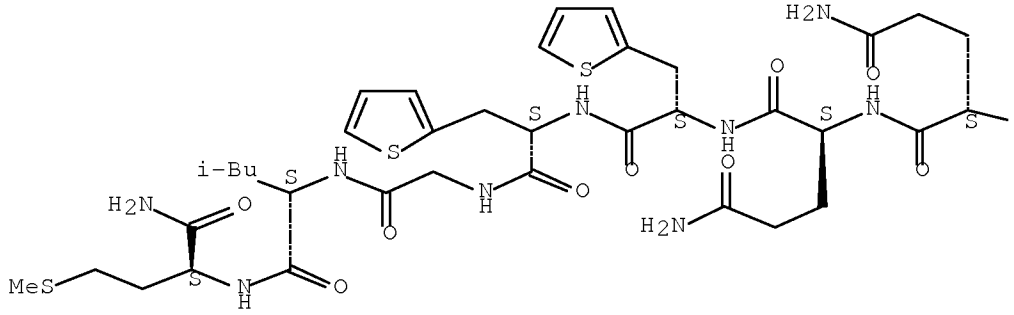
PAGE 1-B



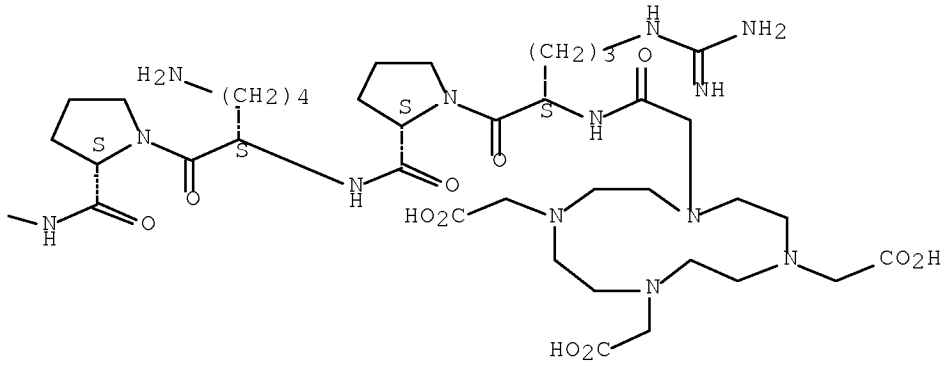
RN 766529-38-8 ZCAPLUS
CN L-Methioninamide, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-3-(2-thienyl)-L-alanyl-3-(2-thienyl)-L-alanylglycyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

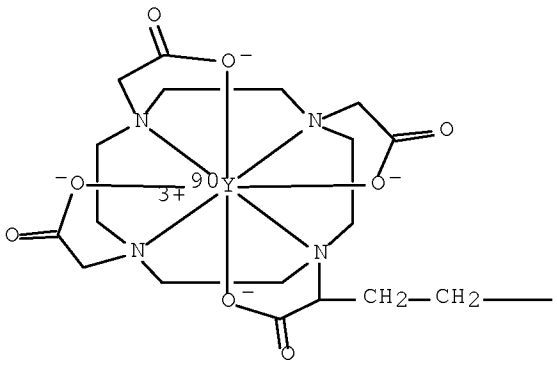


IT 767340-54-5P 767340-55-6P 767340-56-7P
767340-57-8P 767340-58-9P 767340-59-0P
767340-60-3P 767340-61-4P 767340-62-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(radiolabeled substance P conjugates for cancer diagnosis and treatment)

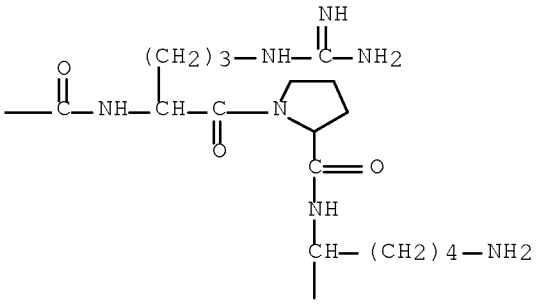
RN 767340-54-5 ZCAPLUS

CN Yttrate(1-)-90Y, [N2-[4-(carboxy-κO)-1-oxo-4-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]butyl]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-L-phenylalanylglycyl-L-leucyl-L-methioninamidato(4-)]- (9CI) (CA INDEX NAME)

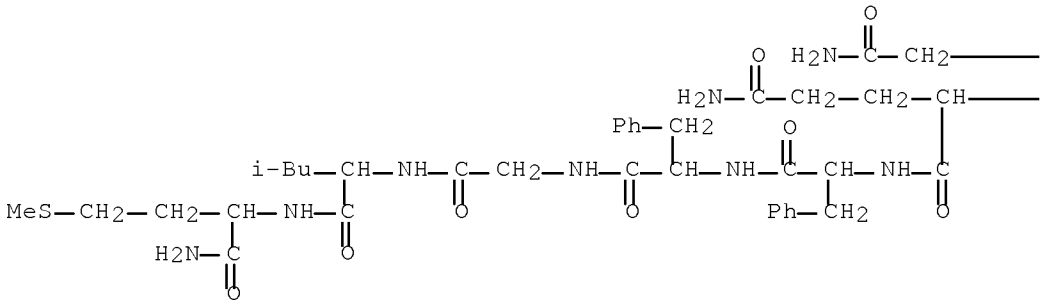
PAGE 1-A



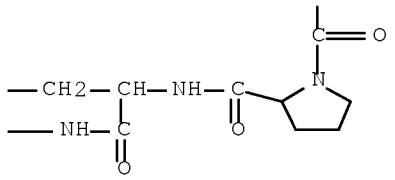
PAGE 1-B



PAGE 2-A



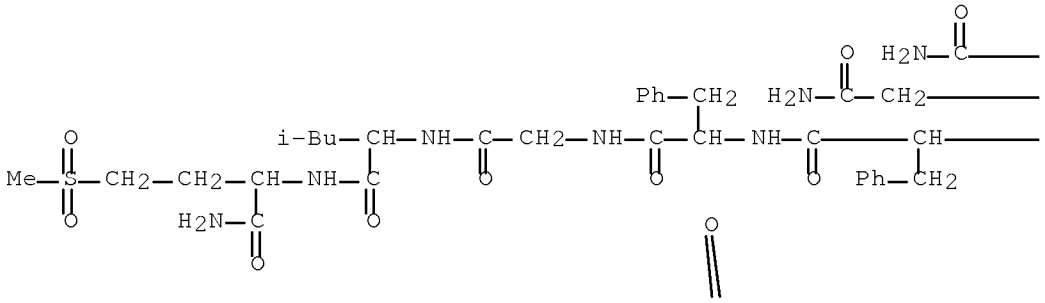
PAGE 2-B



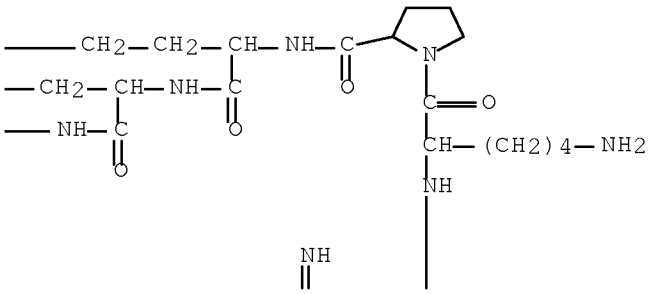
RN 767340-55-6 ZCAPLUS

CN Indium-111In, [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-11-[(2S)-2-amino-4-(methylsulfonyl)butanamide]substance P-ato(3-)]- (9CI) (CA INDEX NAME)

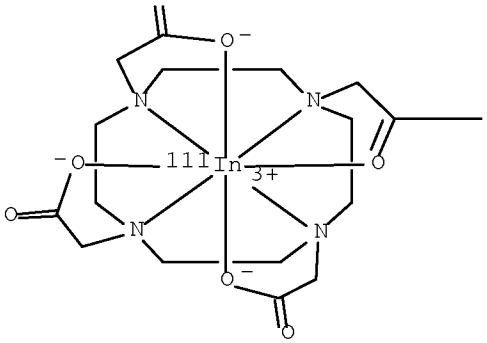
PAGE 1-A



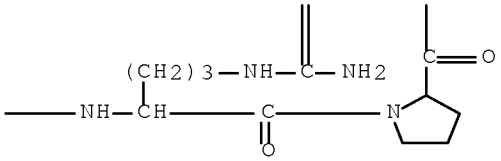
PAGE 1-B



PAGE 2-A



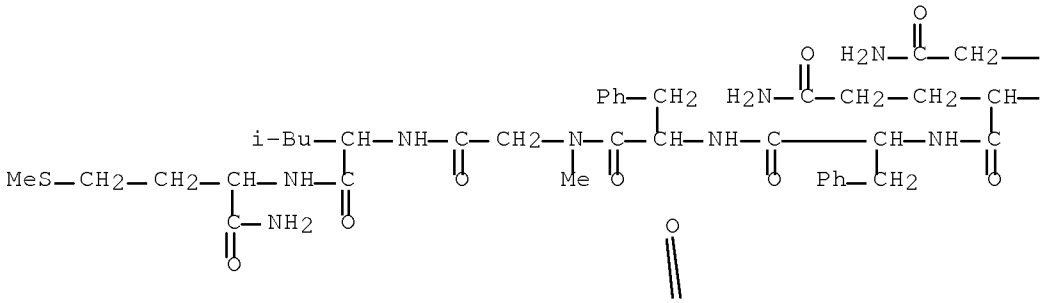
PAGE 2-B



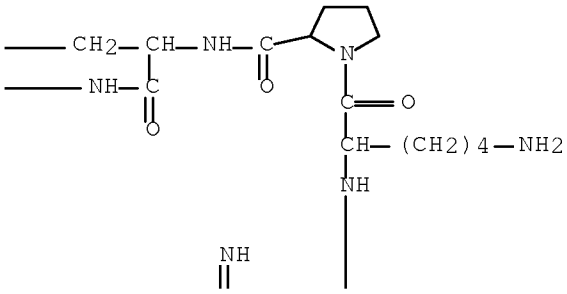
RN 767340-56-7 ZCAPLUS

CN Indium-111In, [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-L-phenylalanyl-N-methylglycyl-L-leucyl-L-methioninamidato(3-)]- (9CI) (CA INDEX NAME)

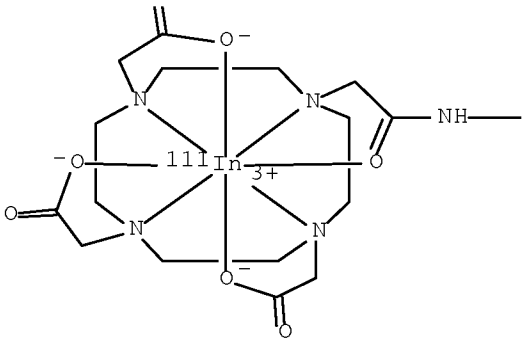
PAGE 1-A



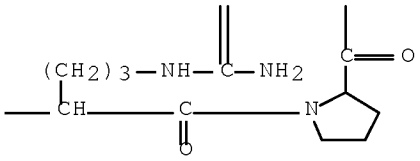
PAGE 1-B



PAGE 2-A



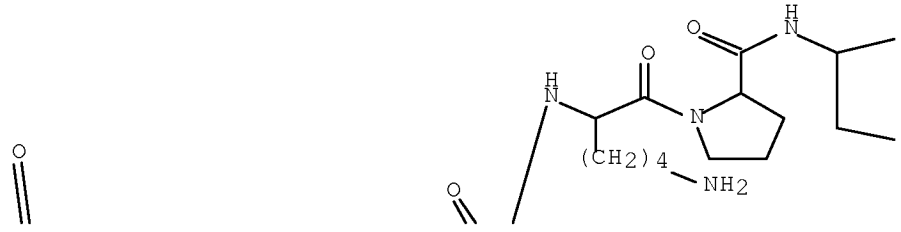
PAGE 2-B



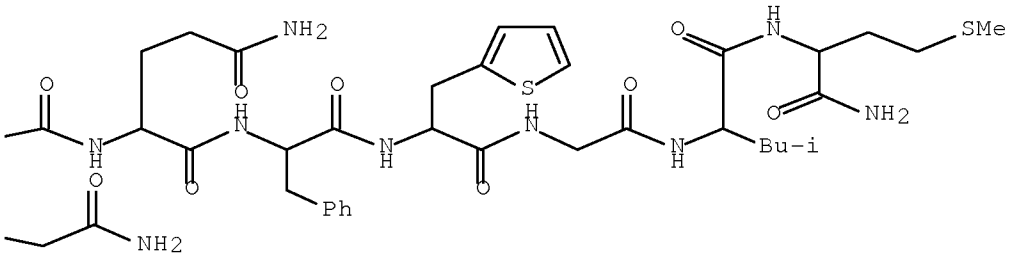
RN 767340-57-8 ZCAPLUS

CN Indium-111In, [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-3-(2-thienyl)-L-alanylglycyl-L-leucyl-L-methioninamidato(3-)]- (9CI) (CA INDEX NAME)

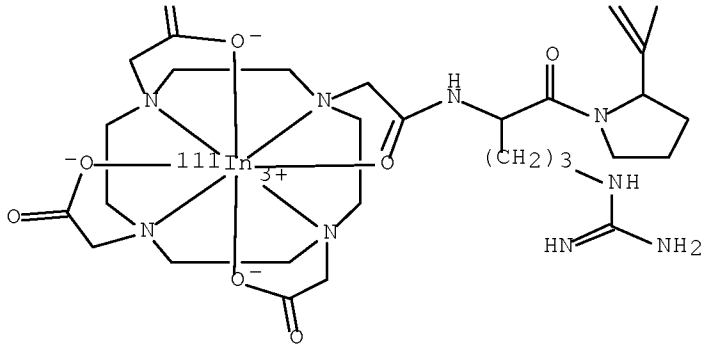
PAGE 1-A



PAGE 1-B



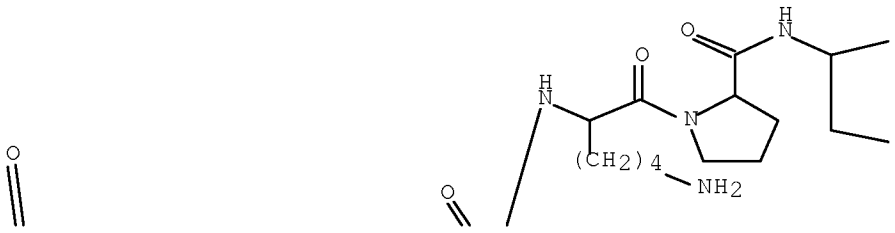
PAGE 2-A



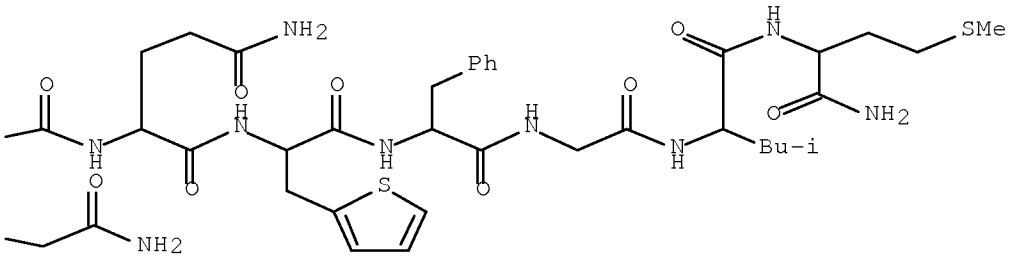
RN 767340-58-9 ZCAPLUS

CN Indium-111In, [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-3-(2-thienyl)-L-alanyl-L-phenylalanylglycyl-L-leucyl-L-methioninamidato(3-)]- (9CI) (CA INDEX NAME)

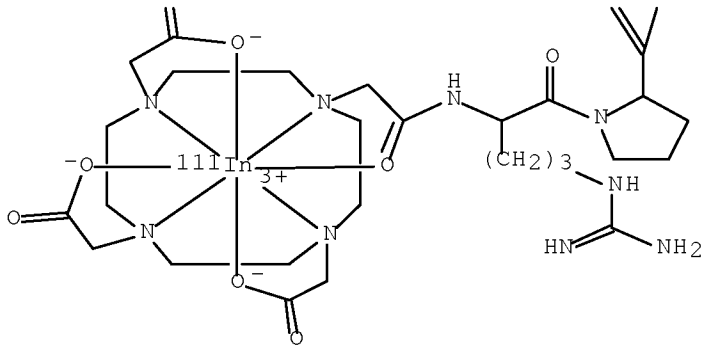
PAGE 1-A



PAGE 1-B



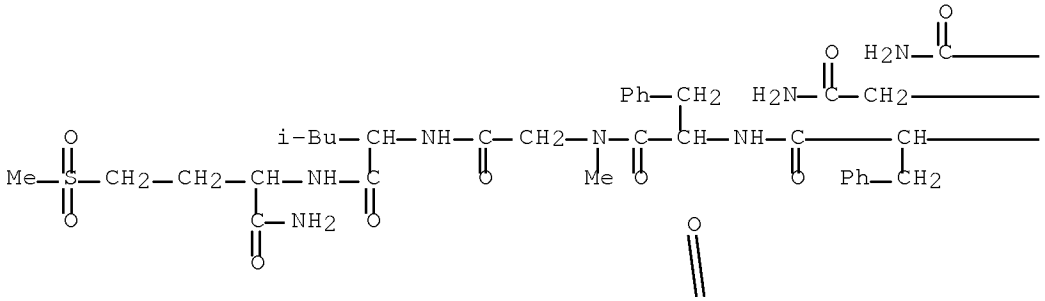
PAGE 2-A



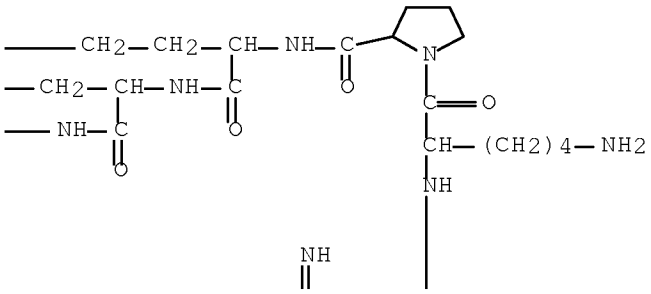
RN 767340-59-0 ZCAPLUS

CN Indium-111In, [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-9-(N-methylglycine)-11-[(2S)-2-amino-4-(methylsulfonyl)butanamide]substance P-ato(3-)]- (9CI) (CA INDEX NAME)

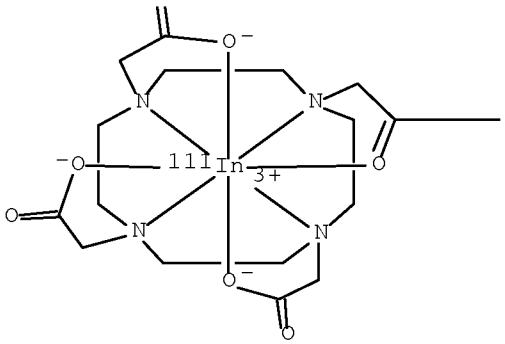
PAGE 1-A



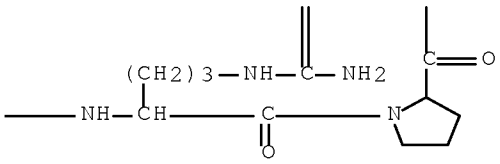
PAGE 1-B



PAGE 2-A



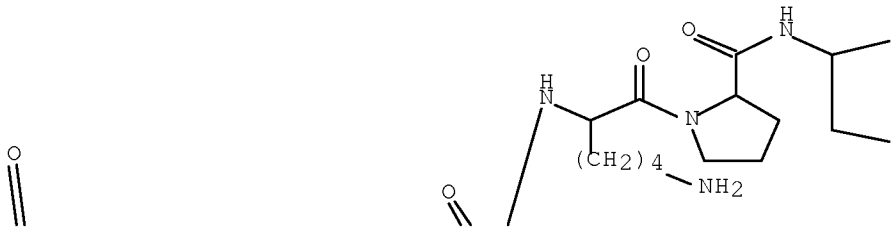
PAGE 2-B



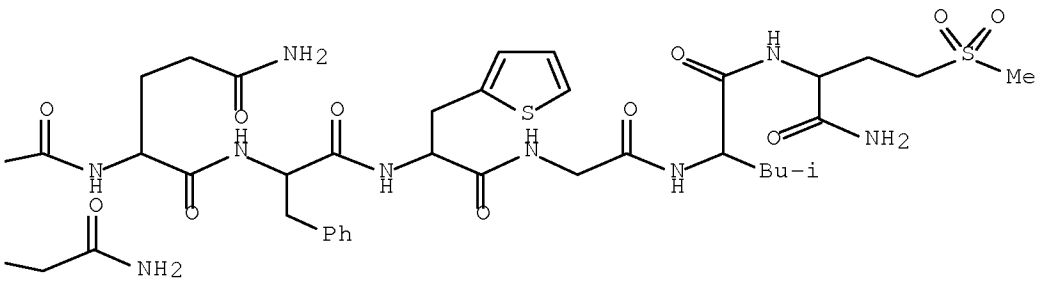
RN 767340-60-3 ZCAPLUS

CN Indium-111In, [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-3-(2-thienyl)-L-alanylglycyl-L-leucyl-(2S)-2-amino-4-(methylsulfonyl)butanamidato(3-)]- (9CI) (CA INDEX NAME)

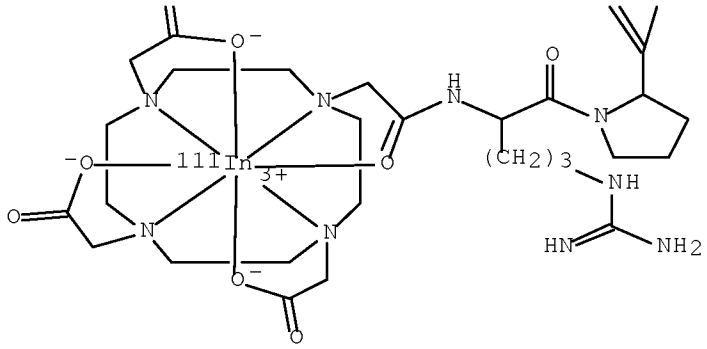
PAGE 1-A



PAGE 1-B



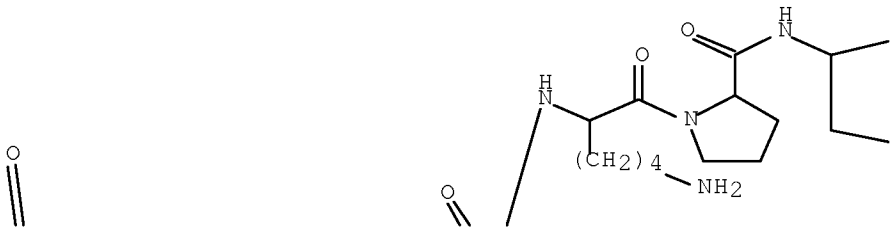
PAGE 2-A



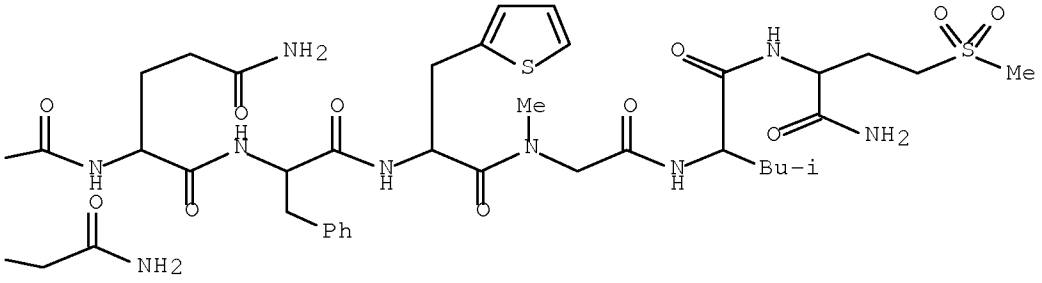
RN 767340-61-4 ZCAPLUS

CN Indium-111In, [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-L-phenylalanyl-3-(2-thienyl)-L-alanyl-N-methylglycyl-L-leucyl-(2S)-2-amino-4-(methylsulfonyl)butanamidato(3-)]- (9CI) (CA INDEX NAME)

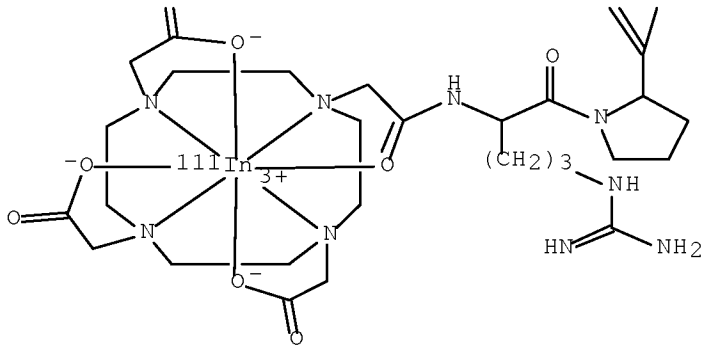
PAGE 1-A



PAGE 1-B



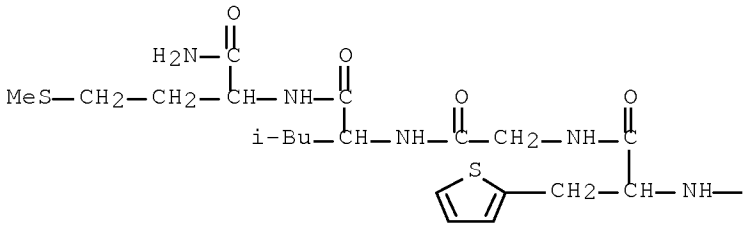
PAGE 2-A



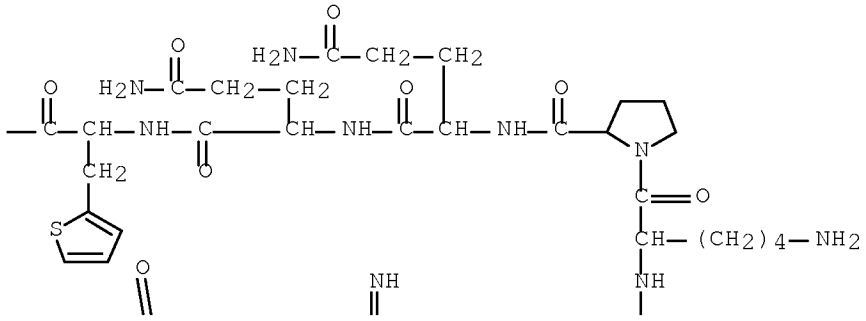
RN 767340-62-5 ZCAPLUS

CN Indium-111In, [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-arginyl-L-prolyl-L-lysyl-L-prolyl-L-glutaminyl-L-glutaminyl-3-(2-thienyl)-L-alanyl-3-(2-thienyl)-L-alanylglycyl-L-leucyl-L-methioninamidato(3-)]- (9CI) (CA INDEX NAME)

PAGE 1-A

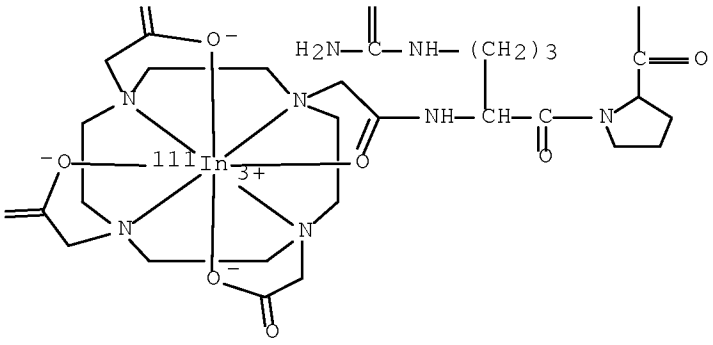


PAGE 1-B



PAGE 2-A

PAGE 2-B



L79 ANSWER 9 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:718526 ZCAPLUS Full-text
DOCUMENT NUMBER: 141:243575
TITLE: Preparation of 1,3,5-trihalo-2,4,6-benzenetricarboxamide N,N,N-tristetraazacyclododecane metal complexes and related compounds as contrast media.
INVENTOR(S): Platzek, Johannes; Weinmann, Hanns-Joachim; Schirmer, Heiko; Martin, Jose Luis; Harto, Juan R.; Riefke, Bjoern
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

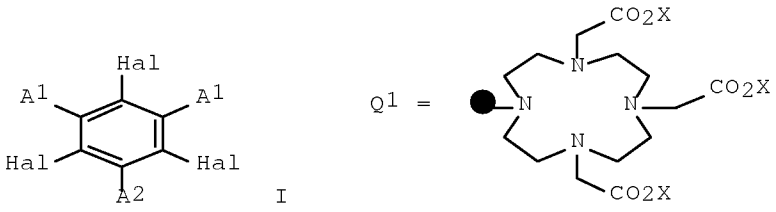
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004074267	A1	20040902	WO 2003-EP14149	20031212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

	KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE	10307759	B3	20041118	DE 2003-10307759	20030219
CA	2516467	A1	20040902	CA 2003-2516467	20031212
AU	2003290032	A1	20040909	AU 2003-290032	20031212
EP	1594851	A1	20051116	EP 2003-782386	20031212
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR	2003018125	A	20060207	BR 2003-18125	20031212
CN	1753878	A	20060329	CN 2003-80109870	20031212
JP	2006514664	T	20060511	JP 2004-568408	20031212
US	2004265236	A1	20041230	US 2004-780887	20040219
US	7208140	B2	20070424		
IN	2005DN03633	A	20070824	IN 2005-DN3633	20050817
MX	2005PA08781	A	20060310	MX 2005-PA8781	20050818
NO	2005004291	A	20051117	NO 2005-4291	20050916
PRIORITY APPLN. INFO.:				DE 2003-10307759 A	20030219
				US 2003-452053P P	20030306
				WO 2003-EP14149 W	20031212

OTHER SOURCE(S): MARPAT 141:243575

GI



AB Title compds. [I; Hal = Br, iodo; A1 = CONR1(CH2)nNR2(COCHZ1NH)mCOCHZ2K, CONR1(CH2)p(CONR2CH2)mCH(OH)CH2K, CH2O(CH2)pCH(OH)CH2K, CH2O(CH2)nNR1(COCHZ1NH)mCOCHZ2K, CH2NR1CO(CHZ1NHCO)mCHZ2K; A2 = A1, NR1CO(NR1)m(CH2)pNR2(COCHZ1NH)mCOCHZ1K; R1, R2 = H, alkyl, hydroxyalkyl; Z1, Z2 = H, Me; n = 2-4; m = 0, 1; p = 1-4; K = Q1; X = H, metal ion of element nos. 20-29, 39, 42, 44, 57-83; ≥2 X = metal ions], were prepared Thus, 2,4,6-triiodo-1,3,5-benzenetricarbonyl trichloride in THF was added to ethylenediamine in THF over 1 h followed by stirring for 14 h to give 70% 2,4,6-triiodo-1,3,5-benzenetricarboxylic acid tris(2-aminoethyl)amide. This was added to a mixture prepared from the Gd complex of 10-[4-carboxy-1-methyl-2-oxo-3-azabutyl]-1,4,7,10- tetraazacyclododecane-1,4,7-triacetic acid, DCC, and N-hydroxysuccinimide in Me2SO to give 73% 2,4,6-triiodo-1,3,5-benzenetricarboxylic acid N,N,N-tris-[3,6-diaza-4,7-dioxo-8-methyloctan-1,8-diyl-[10-[1,4,7- tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane, Gd complex]]]amide. The latter was used for CT imaging of rat blood vessels and kidneys.

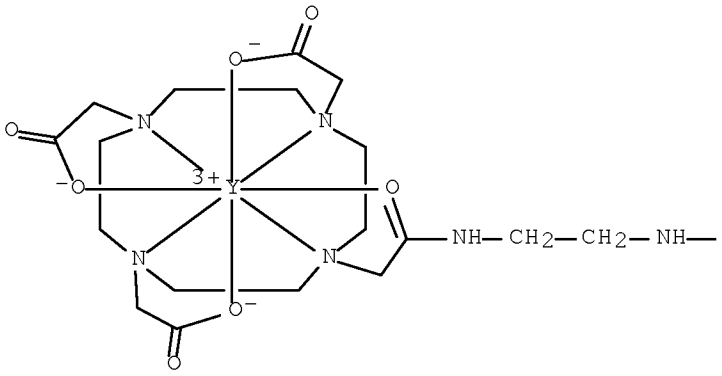
IC ICM C07D257-02
ICS A61K049-04; A61K049-06; A61K051-04; A61K049-08

CC 28-23 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 63, 78

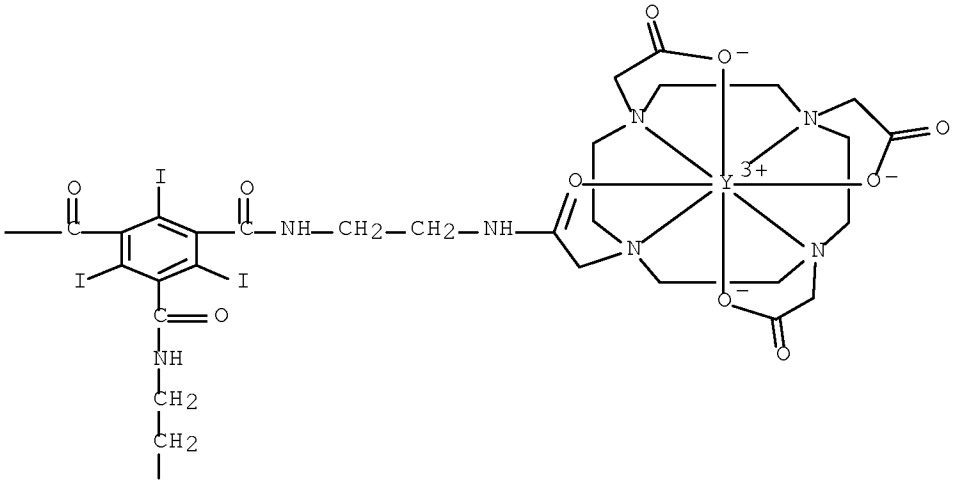
IT Musculoskeletal diseases
(tumor imaging; preparation of trihalobenzenetricarboxamide tristetraazacyclododecane metal complexes and related compds. as

contrast media)
IT 7429-91-6DP, Dysprosium, complexes 7439-89-6DP, Iron, complexes
7439-96-5DP, Manganese, complexes 7440-53-1DP, Europium, complexes
7440-54-2DP, Gadolinium, complexes 753020-30-3P 753020-31-4P
753020-32-5P 753020-33-6P 753020-34-7P 753020-35-8P
753020-36-9P 753020-37-0P 753020-39-2P 753020-40-5P 753020-42-7P
753020-43-8P 753020-44-9P 753020-45-0P 753020-46-1P
753020-49-4P 753020-51-8P 753020-53-0P
753020-56-3P 753020-59-6P 753020-61-0P
753020-63-2P 753020-65-4P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of trihalobenzenetricarboxamide tristetraazacyclododecane metal
complexes and related compds. as contrast media)
IT 14321-26-7P 88285-82-9P 138884-10-3P 138884-11-4P 400894-66-8P
425367-31-3P 425367-47-1P 425367-60-8P 752252-78-1P 752252-79-2P
752252-80-5P 752252-81-6P 752252-82-7P 752252-83-8P
752252-84-9P 752252-85-0P 752252-86-1P 752252-87-2P
752252-88-3P 752252-89-4P 752252-90-7P 752252-91-8P 752252-92-9P
752252-93-0P 752252-94-1P 752252-95-2P 752252-96-3P 752252-97-4P
752252-98-5P 752252-99-6P 752253-00-2P 752253-01-3P 752253-02-4P
752253-03-5P 752253-04-6P 752253-05-7P 752253-06-8P 752253-07-9P
752253-08-0P 752253-09-1P 752253-10-4P 752253-11-5P 752253-12-6P
752253-13-7P 752253-14-8P 752253-15-9P 752253-16-0P 752253-17-1P
752253-18-2P 752253-19-3P 752253-20-6P 752253-21-7P 752253-22-8P
752253-23-9P 752253-24-0P 752253-25-1P 752253-26-2P
752253-27-3P 752253-28-4P 752253-29-5P 752253-30-8P
752253-31-9P 752253-32-0P 752253-33-1P 752253-34-2P
752253-35-3P 752253-36-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of trihalobenzenetricarboxamide tristetraazacyclododecane metal
complexes and related compds. as contrast media)
IT 753020-32-5P 753020-33-6P 753020-49-4P
753020-51-8P 753020-53-0P 753020-56-3P
753020-59-6P 753020-61-0P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of trihalobenzenetricarboxamide tristetraazacyclododecane metal
complexes and related compds. as contrast media)
RN 753020-32-5 ZCAPLUS
CN Yttrium, [μ3-[[10,10',10''-[(2,4,6-triiodo-1,3,5-benzenetriyl)tris[carbonylimino-2,1-ethanediylimino[2-(oxo-κO)-2,1-ethanediyl]]]tris[1,4,7,10-tetraazacyclododecane-1,4,7-triacetato-κN1,κN4,κN7,κN10,κO1,κO4,κO7]](9-)]]tri- (9CI) (CA INDEX NAME)

PAGE 1-A

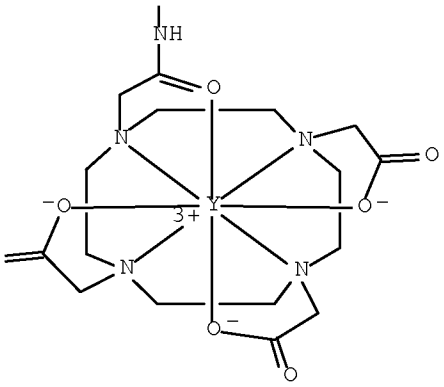


PAGE 1-B



PAGE 2-A

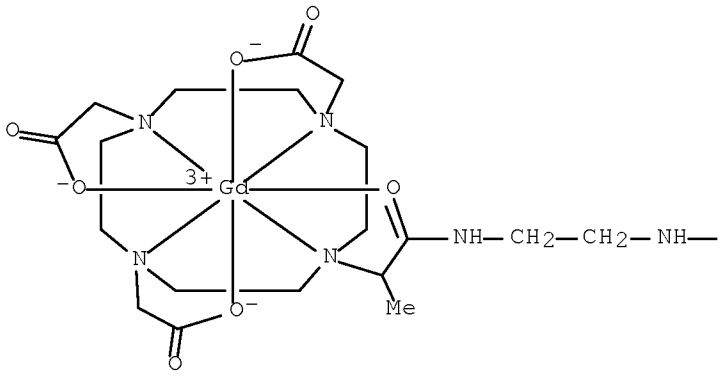
PAGE 2-B



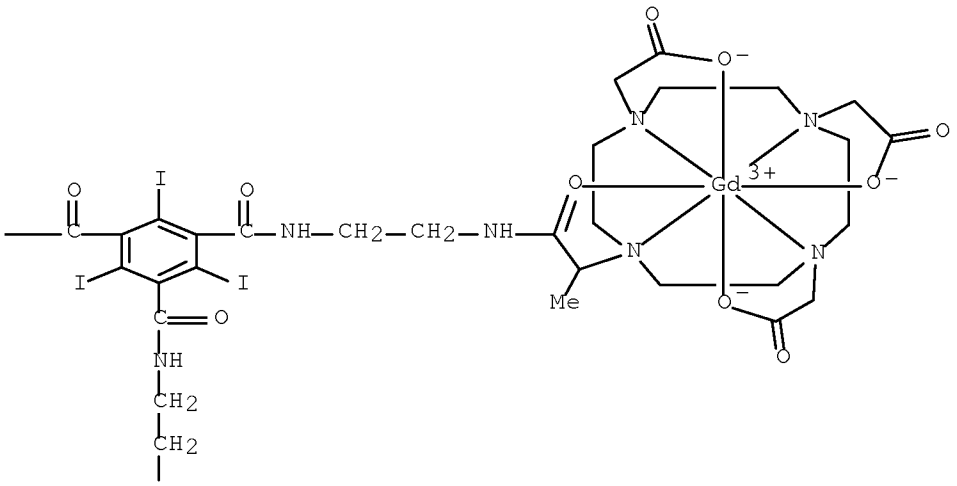
RN 753020-33-6 ZCAPLUS

CN Gadolinium, [μ3-[[10,10',10''-[(2,4,6-triiodo-1,3,5-benzenetriyl)tris[carbonylimino-2,1-ethanediylimino[1-methyl-2-(oxo-κO)-2,1-ethanediyl]]]tris[1,4,7,10-tetraazacyclododecane-1,4,7-triacetato-κN1,κN4,κN7,κN10,κO1,κO4,.k appa.O7]](9-)]]tri- (9CI) (CA INDEX NAME)

PAGE 1-A



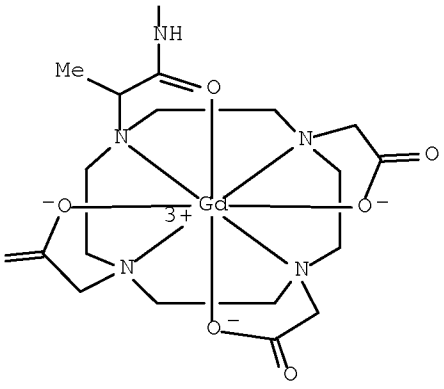
PAGE 1-B



PAGE 2-A

O=

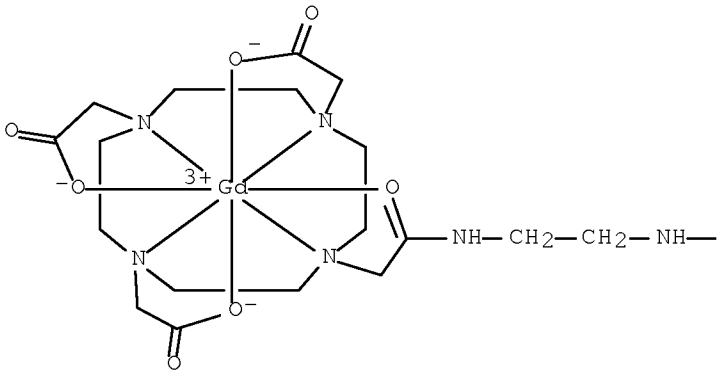
PAGE 2-B



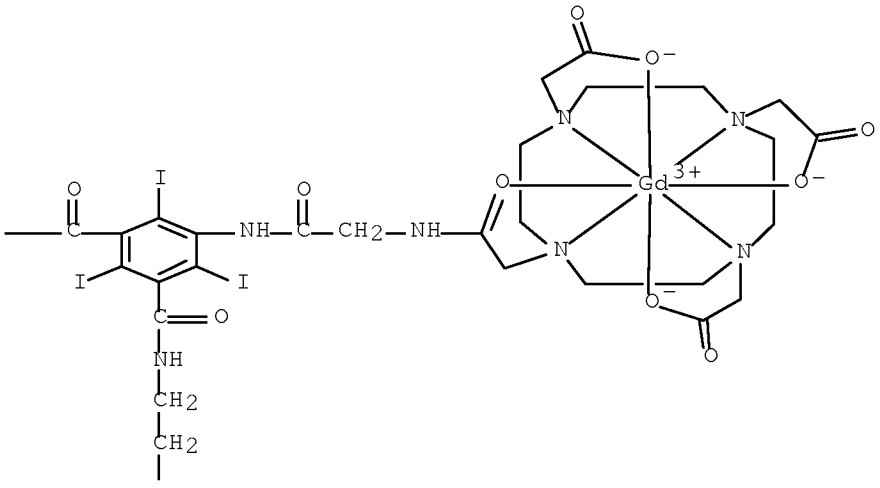
RN 753020-49-4 ZCAPLUS

CN Gadolinium, [μ3-[[10,10'-[[2,4,6-triiodo-5-[[[[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]amino]acetyl]amino]-1,3-phenylene]bis[carbonylimino-2,1-ethanediylimino[2-(oxo-κO)-2,1-ethanediyl]]]bis[1,4,7,10-tetraazacyclododecane-1,4,7-triacetato-κN1,κN4,κN7,.kappa.N10,κO1,κO4,κO7]](9-)]]tri- (9CI) (CA INDEX NAME)

PAGE 1-A



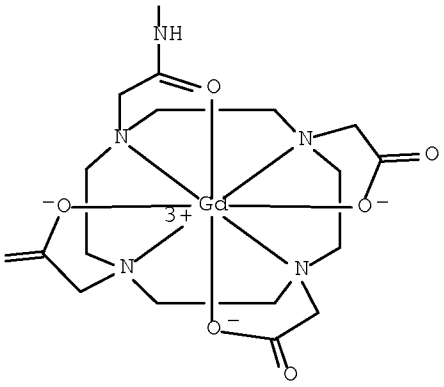
PAGE 1-B



PAGE 2-A

O═

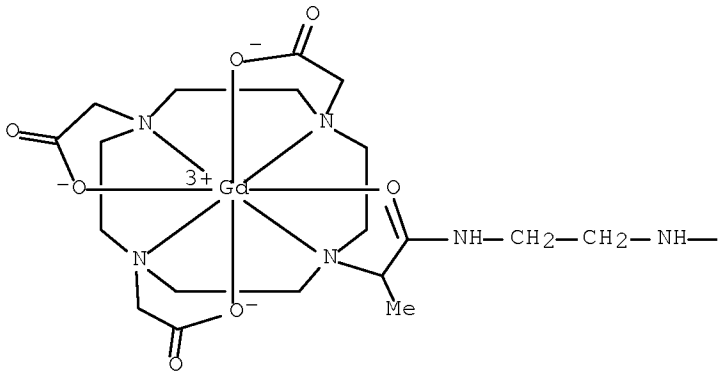
PAGE 2-B



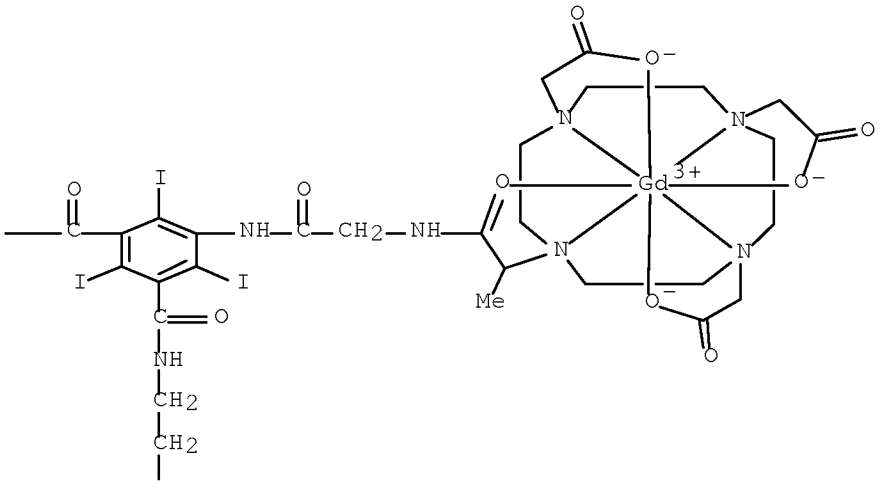
RN 753020-51-8 ZCAPLUS

CN Gadolinium, [μ3-[[10,10'-[[2,4,6-triiodo-5-[[[[1-(oxo-κO)-2-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]propyl]amino]acetyl]amino]-1,3-phenylene]bis[carbonylimino-2,1-ethanediylimino[1-methyl-2-(oxo-κO)-2,1-ethanediyl]]]bis[1,4,7,10-tetraazacyclododecane-1,4,7-triacetato-κN1,κN4,κN7,κN10,κO1,κO4,κO7]](9-)]]tri- (9CI) (CA INDEX NAME)

PAGE 1-A

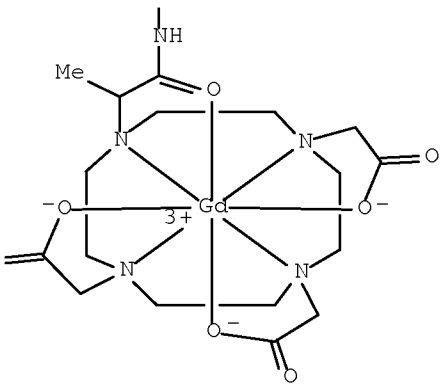


PAGE 1-B



PAGE 2-A

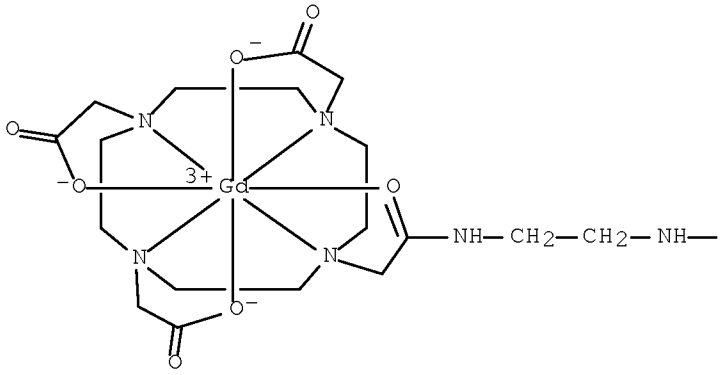
PAGE 2-B



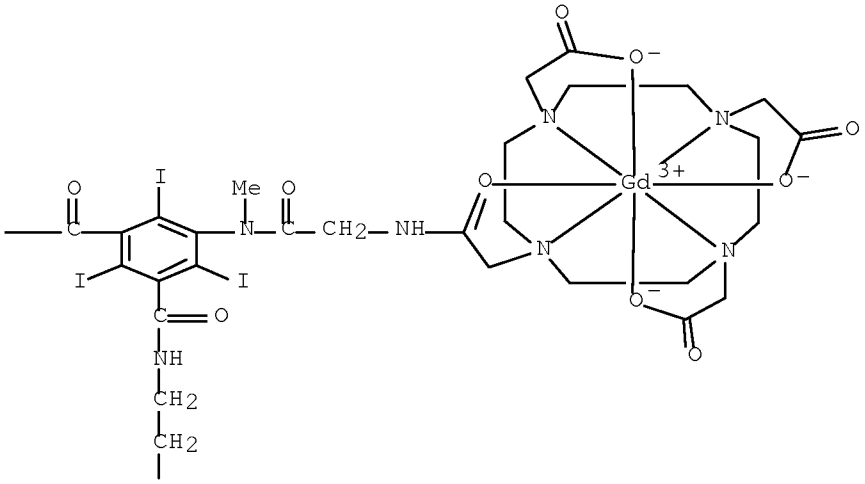
RN 753020-53-0 ZCAPLUS

CN Gadolinium, [μ3-[[10,10'-[[2,4,6-triiodo-5-[methyl[[[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]amino]acetyl]amino]-1,3-phenylene]bis[carbonylimino-2,1-ethanediylimino[2-(oxo-κO)-2,1-ethanediyl]]]bis[1,4,7,10-tetraazacyclododecane-1,4,7-triacetato-κN1,κN4,κN7,.kappa.N10,κO1,κO4,κO7]](9-)]]tri- (9CI) (CA INDEX NAME)

PAGE 1-A

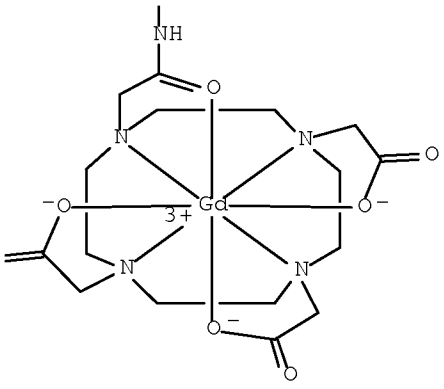


PAGE 1-B



PAGE 2-A

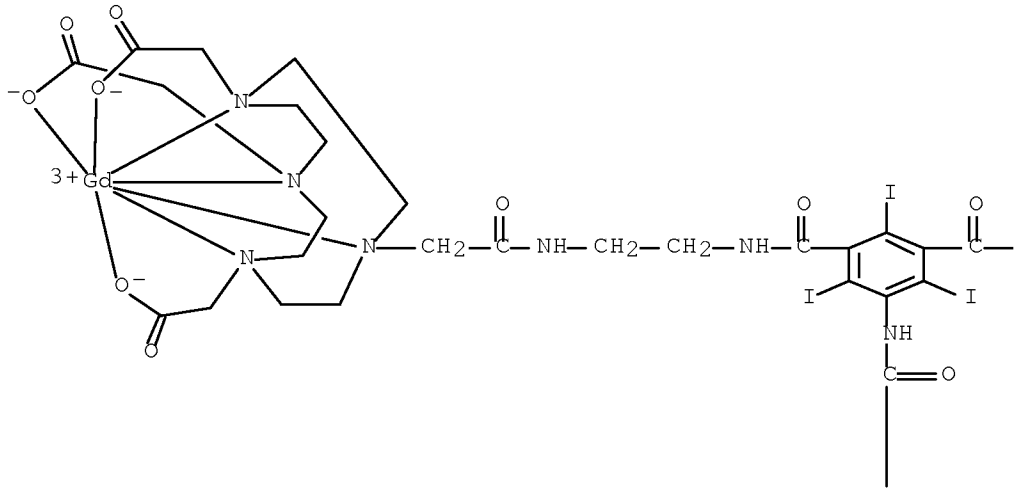
PAGE 2-B



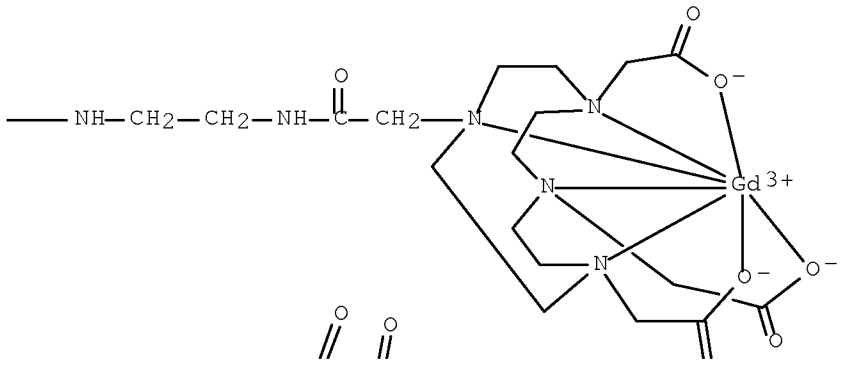
RN 753020-56-3 ZCAPLUS

CN Gadolinium, [μ3-[[10,10'-[[2,4,6-triiodo-5-[[[[2-[[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl]amino]ethyl]amino]carbonyl]amino]-1,3-phenylene]bis[carbonylimino-2,1-ethanediylimino[2-(oxo-κO)-2,1-ethanediyl]]]bis[1,4,7,10-tetraazacyclododecane-1,4,7-triacetato-κN1,κN4,κN7,κN10,κO1,κO4,.kappa.O7]](9-)]]tri- (9CI) (CA INDEX NAME)

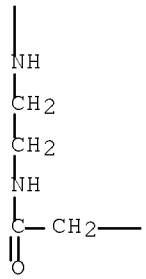
PAGE 1-A



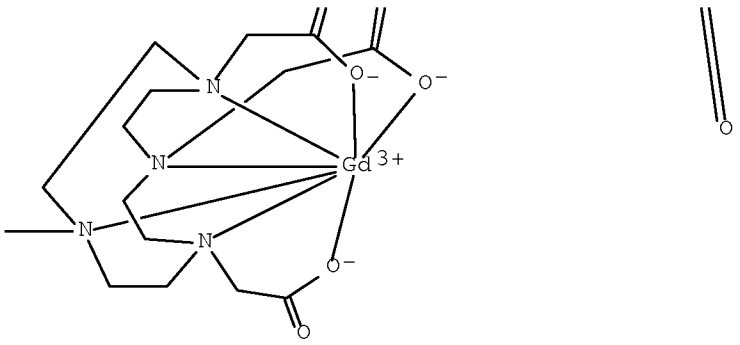
PAGE 1-B



PAGE 2-A



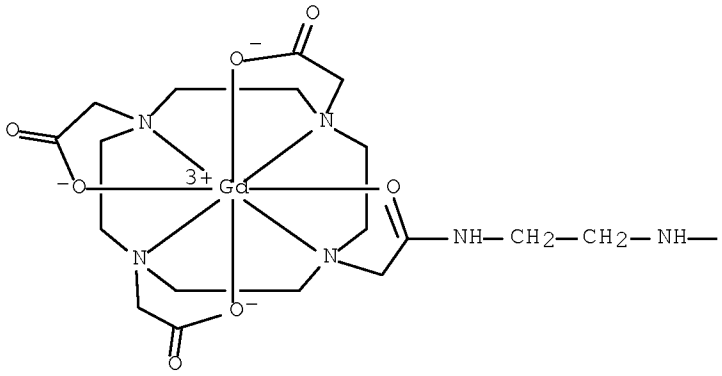
PAGE 2-B



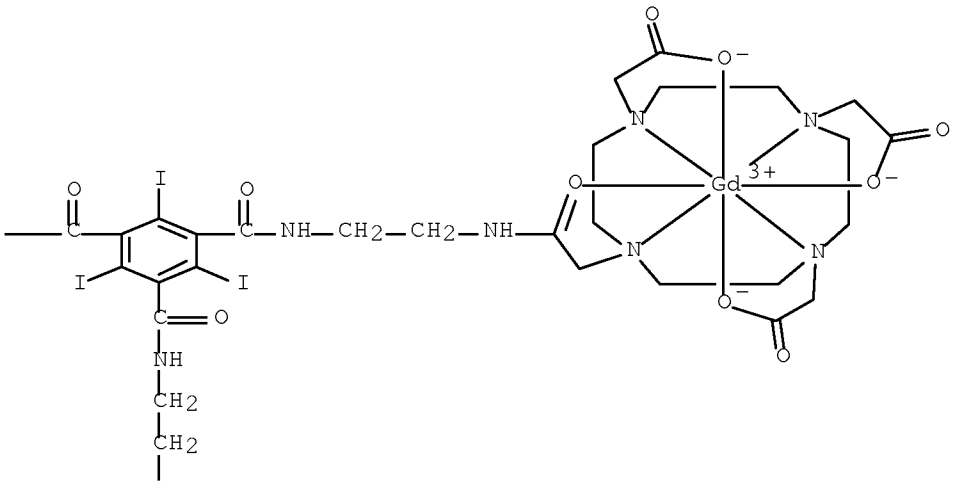
RN 753020-59-6 ZCAPLUS

CN Gadolinium, [μ3-[[10,10',10''-[(2,4,6-triiodo-1,3,5-benzenetriyl)tris[carbonylimino-2,1-ethanediylimino[2-(oxo-κO)-2,1-ethanediyl]]]tris[1,4,7,10-tetraazacyclododecane-1,4,7-triacetato-κN1,κN4,κN7,κN10,κO1,κO4,κO7]](9-)]]tri- (9CI) (CA INDEX NAME)

PAGE 1-A

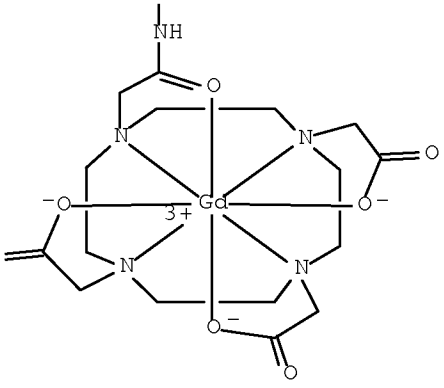


PAGE 1-B



PAGE 2-A

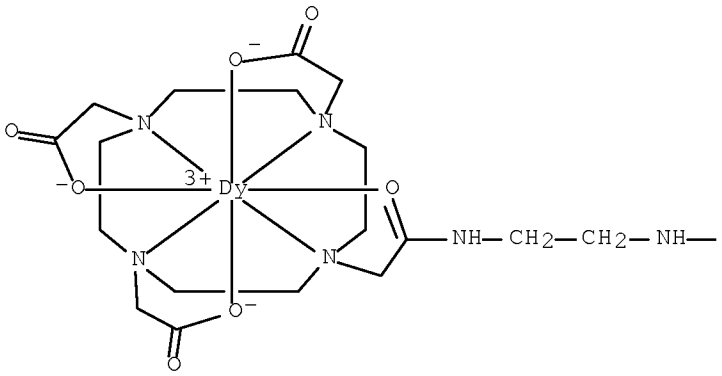
PAGE 2-B



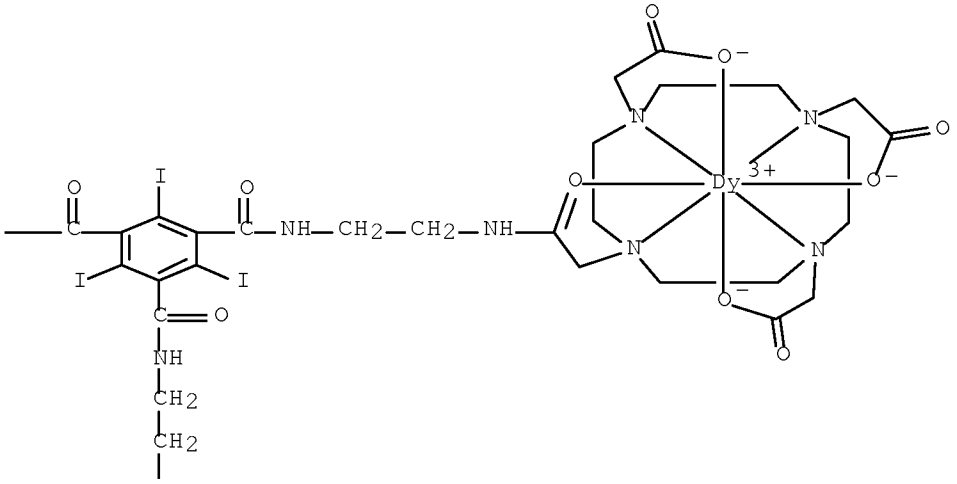
RN 753020-61-0 ZCAPLUS

CN Dysprosium, [μ3-[[10,10',10''-[(2,4,6-triiodo-1,3,5-benzenetriyl)tris[carbonylimino-2,1-ethanediylimino[2-(oxo-κO)-2,1-ethanediyl]]]tris[1,4,7,10-tetraazacyclododecane-1,4,7-triacetato-κN1,κN4,κN7,κN10,κO1,κO4,κO7]](9-)]]tri- (9CI) (CA INDEX NAME)

PAGE 1-A



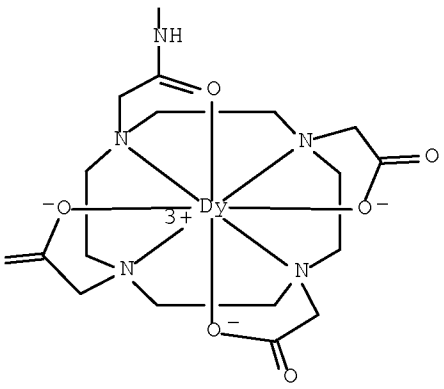
PAGE 1-B



PAGE 2-A

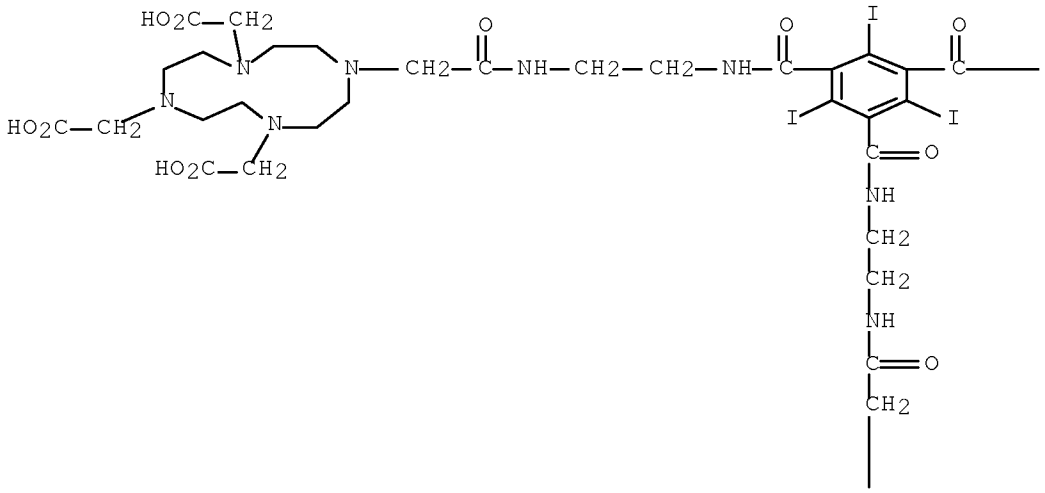
O═

PAGE 2-B

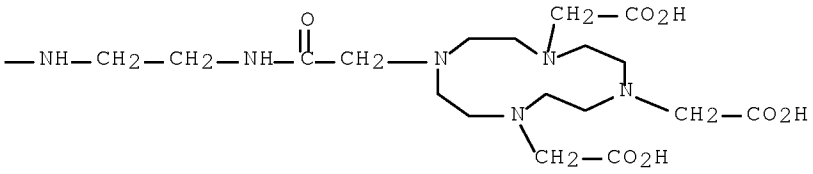


IT 752252-82-7P 752252-85-0P 752253-24-0P
752253-27-3P 752253-32-0P 752253-36-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of trihalobenzenetricarboxamide tristetraazacyclododecane metal
complexes and related compds. as contrast media)
RN 752252-82-7 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10',10''-[(2,4,6-triiodo-1,3,5-benzenetriyl)tris[carbonylimino-2,1-ethanediylimino(2-oxo-2,1-ethanediyl)]]tris- (9CI) (CA INDEX NAME)

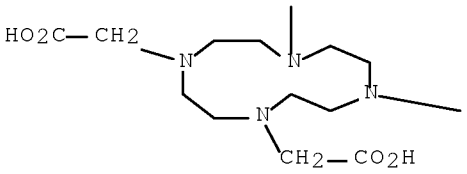
PAGE 1-A



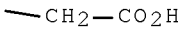
PAGE 1-B



PAGE 2-A



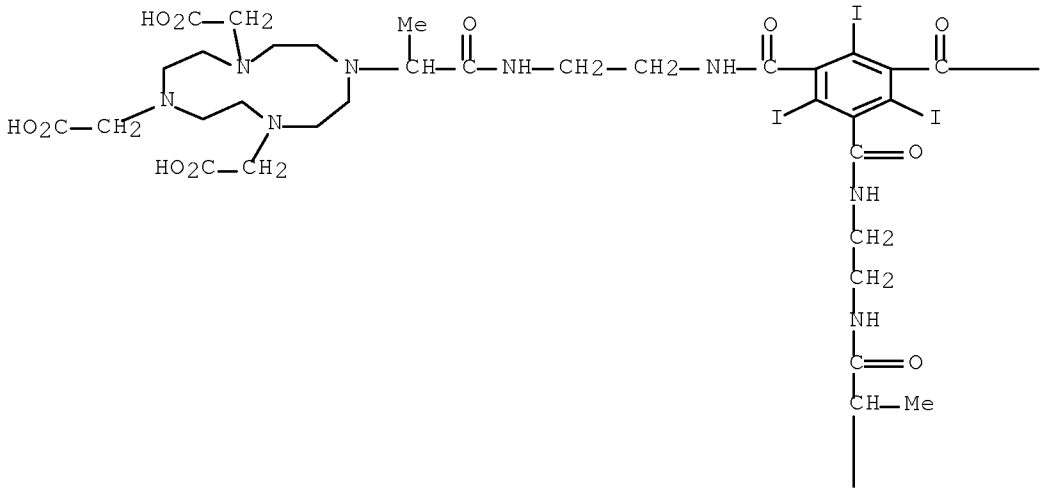
PAGE 2-B



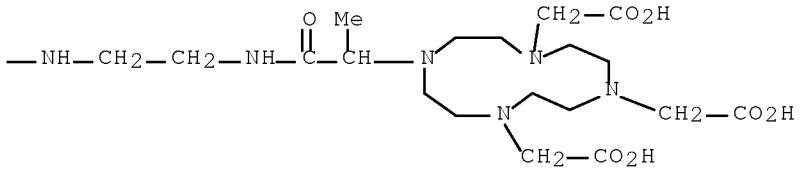
RN 752252-85-0 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10',10''-[(2,4,6-triiodo-1,3,5-benzenetriyl)tris[carbonylimino-2,1-ethanediylimino(1-methyl-2-oxo-2,1-ethanediyl)]]tris- (9CI) (CA INDEX NAME)

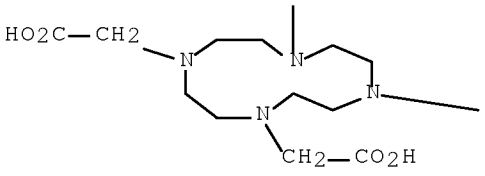
PAGE 1-A



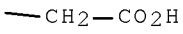
PAGE 1-B



PAGE 2-A

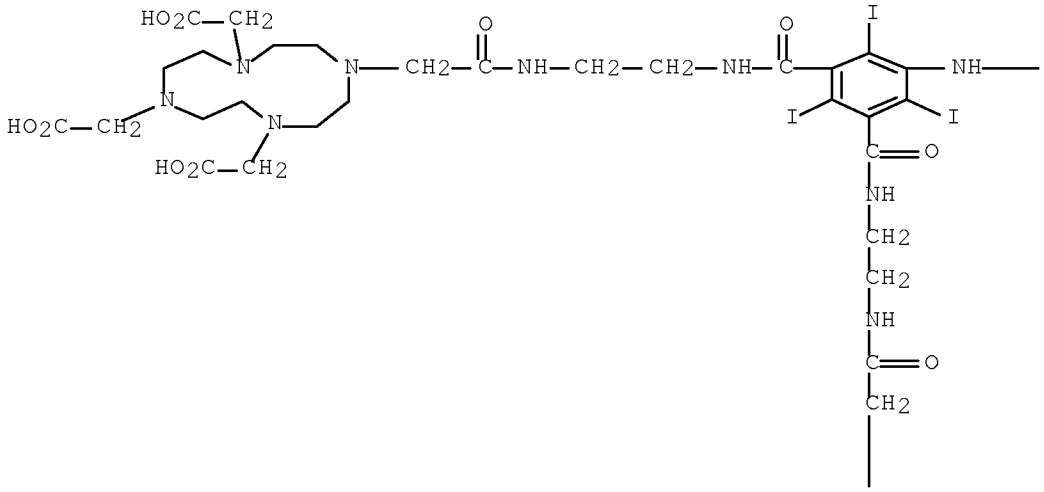


PAGE 2-B

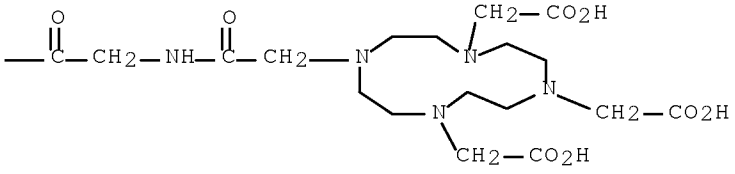


RN 752253-24-0 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[(2,4,6-triiodo-5-[[[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]acetyl]amino]-1,3-phenylene)bis[carbonylimino-2,1-ethanediylimino(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

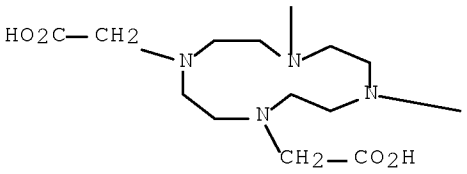
PAGE 1-A



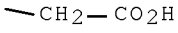
PAGE 1-B



PAGE 2-A



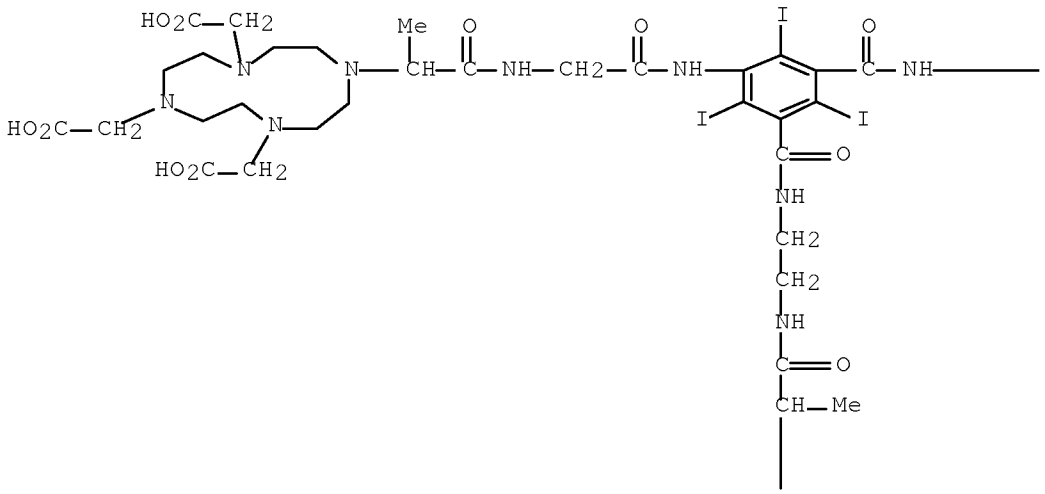
PAGE 2-B



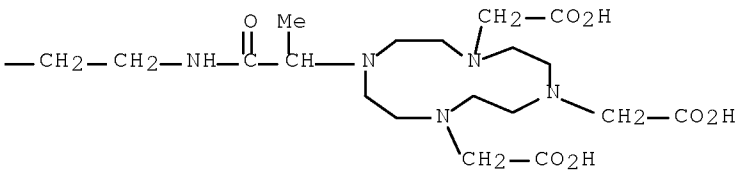
RN 752253-27-3 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[(2,4,6-triiodo-5-[[[[1-oxo-2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]propyl]amino]acetyl]amino]-1,3-phenylene)bis[carbonylimino-2,1-ethanediylimino(1-methyl-2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

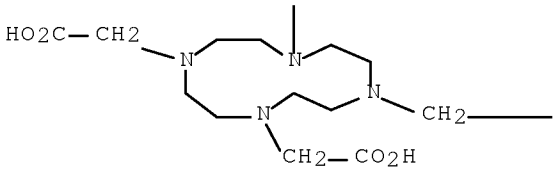
PAGE 1-A



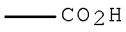
PAGE 1-B



PAGE 2-A



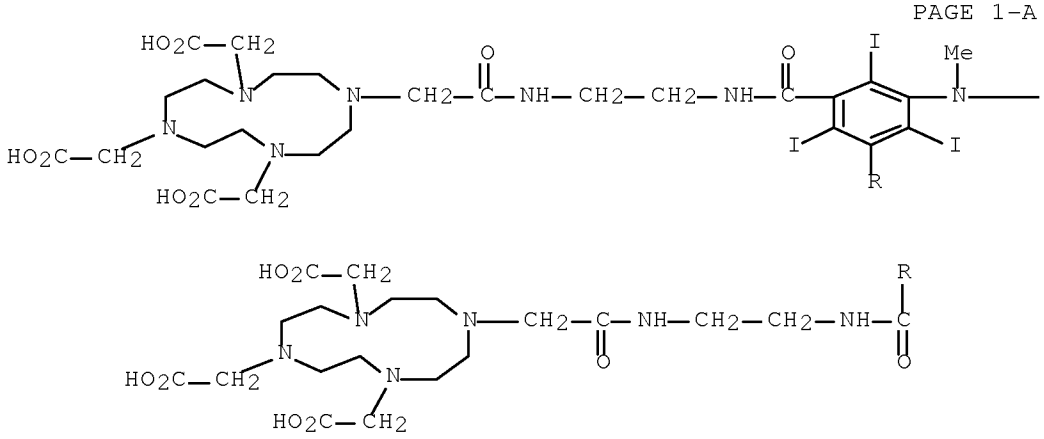
PAGE 2-B



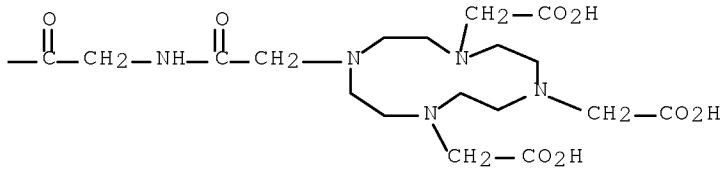
RN 752253-32-0 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[(2,4,6-triiodo-5-[methyl[[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]acetyl]amino]-1,3-phenylene)bis[carbonylimino-2,1-ethanediylimino(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



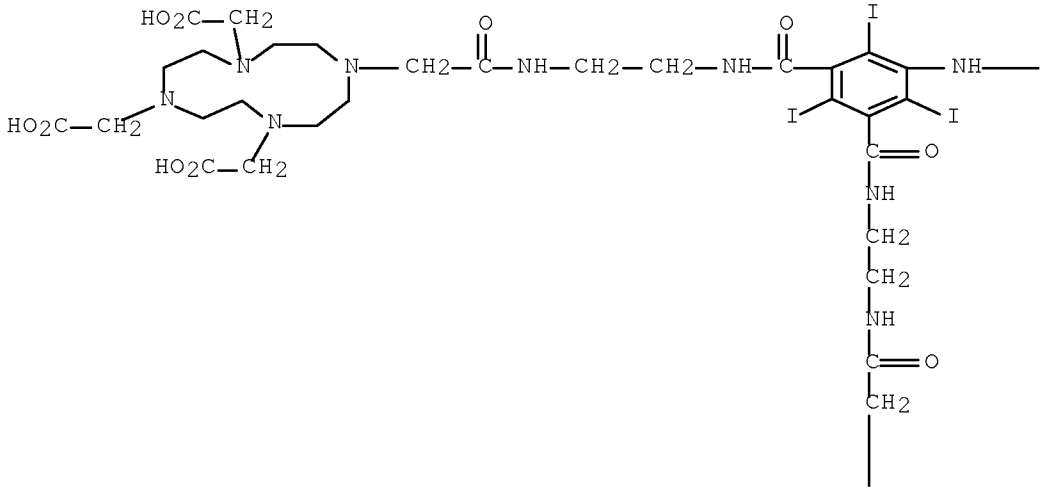
PAGE 1-B



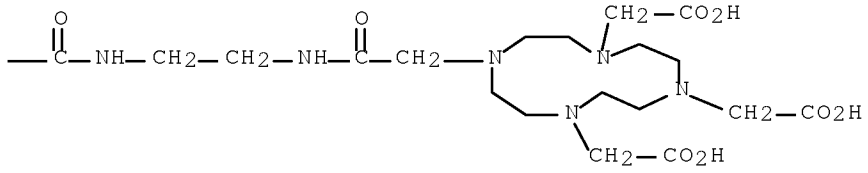
RN 752253-36-4 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[(2,4,6-triiodo-5-[[[[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]carbonyl]amino]-1,3-phenylene)bis[carbonylimino-2,1-ethanediylimino(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

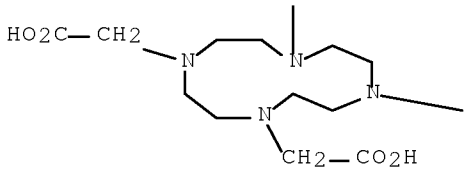
PAGE 1-A



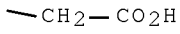
PAGE 1-B



PAGE 2-A



PAGE 2-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 10 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:432097 ZCAPLUS Full-text
DOCUMENT NUMBER: 141:153123
TITLE: In Vitro and in Vivo Comparison of Human Escherichia coli Heat-Stable Peptide Analogues Incorporating the 111In-DOTA Group and Distinct Linker Moieties
AUTHOR(S): Giblin, Michael F.; Gali, Hariprasad; Sieckman, Gary L.; Owen, Nellie K.; Hoffman, Timothy J.; Forte, Leonard R.; Volkert, Wynn A.
CORPORATE SOURCE: Research Service, Harry S. Truman Memorial Veterans' Administration Hospital, Columbia, MO, 65201, USA
SOURCE: Bioconjugate Chemistry (2004), 15(4), 872-880
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three human Escherichia coli heat-stable peptide (STh) analogs, each containing a DOTA chelating group, were synthesized by SPPS and oxidative refolding and compared in in vitro and in vivo systems. One analog, DOTA-F19-STh(1-19), contains an N-terminal DOTA group attached via an amide bond linkage to an STh moiety which is essentially wild-type except for a Tyr to Phe alteration at position 19 of the mol. A second analog, DOTA-R1,4,F19-STh(1-19), differs from the first in that asparagine residues in positions 1 and 4 have been altered to arginine residues in order to examine the effect of pos. charged groups in the linker domain. A third analog, DOTA-11AUN-F19-STh(1-19), differs from the first in that it incorporates an 11-aminoundecanoic acid spacer group between the DOTA group and the first asparagine residue. In vitro competitive binding assays utilizing T-84 human colon cancer cells demonstrated that significant alterations to the N-terminal region of the STh mol. were well tolerated and did not significantly affect binding affinity of STh for the guanylyl cyclase C (GC-C) receptor.

Internalization and efflux studies of the indium-labeled species demonstrated that inclusion of pos. charge in the linker moiety inhibits internalization of the compound within tumor cells. The characteristics of the three analogs were compared in an in vivo model utilizing T-84 human colon cancer cell xenografts in SCID mice. Clearance of all analogs was rapid, primarily via renal excretion into the urine, with >89% ID excreted into the urine at 1 h pi for all analogs. The 111In-DOTA-R1,4,F19-STh(1-19) and 111In-DOTA-11AUN-F19-STh(1-19) analogs both had longer residence times in the blood than did the 111In-DOTA-F19-STh(1-19) analog, probably accounting for increased %ID/g values for tumors and nontarget tissues at 1 h pi. At 4 h pi, significant differences between analogs were only seen with respect to metabolic routes of excretion, indicating that increased blood residence time did not result in increased tumor residualization. Reduction of hepatic uptake of these compds., however, could have significance in the development of agents for the imaging of hepatic metastases. The ability to manipulate in vivo pharmacodynamics and tumor uptake of radiolabeled STh peptides through modification of linker moieties is under continuing investigation in order to produce optimal imaging and therapeutic radiopharmaceuticals.

CC 8-9 (Radiation Biochemistry)

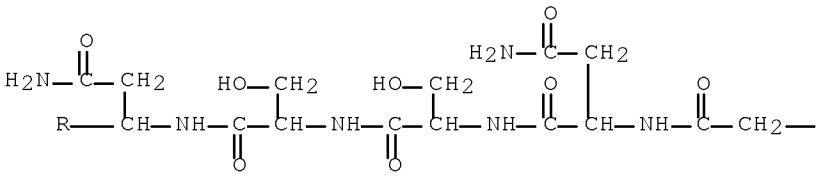
IT 415706-07-9P 728914-72-5P 728914-74-7P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in vitro and in vivo comparison of human E. coli heat-stable peptide analogs incorporating 111In-DOTA group and distinct linker moieties)

IT 415706-07-9P 728914-72-5P 728914-74-7P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(in vitro and in vivo comparison of human E. coli heat-stable peptide analogs incorporating 111In-DOTA group and distinct linker moieties)

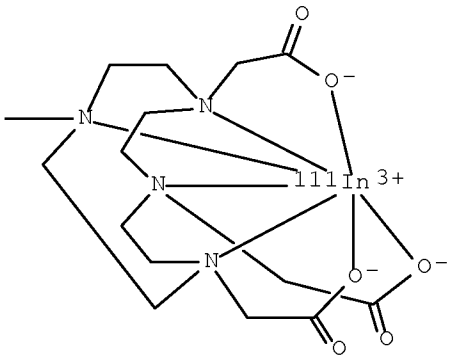
RN 415706-07-9 ZCAPLUS

CN Indate(2-)-111In, [N2-[2-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl]-L-asparaginyl-L-seryl-L-seryl-L-asparaginyl-L-tyrosyl-L-cysteinyl-L-cysteinyl-L-α-glutamyl-L-leucyl-L-cysteinyl-L-cysteinyl-L-asparaginyl-L-prolyl-L-alanyl-L-cysteinyl-L-threonylglycyl-L-cysteinyl-L-phenylalanine cyclic (6→11),(7→15),(10→18)-tris(disulfidato)(5-)]-, hydrogen (1:2) (CA INDEX NAME)

PAGE 1-A

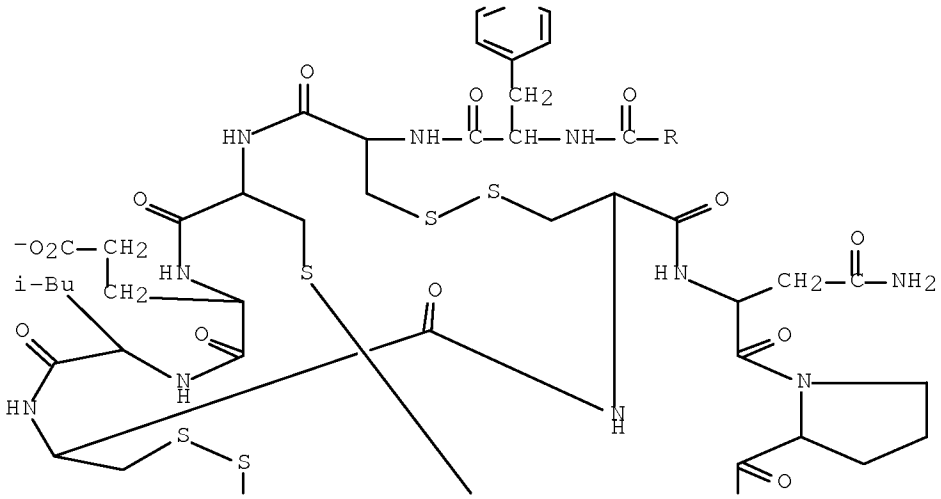


PAGE 1-B



PAGE 3-B

PAGE 4-B

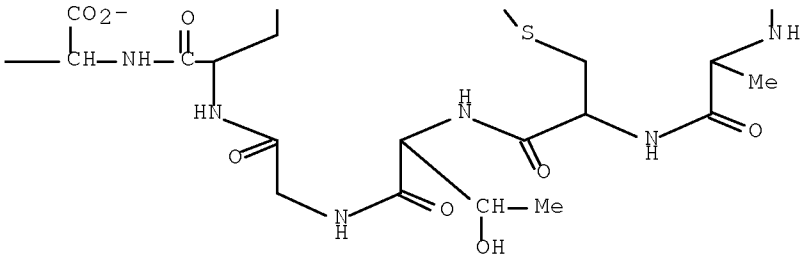


PAGE 5-A

Ph—CH2—

●2 H+

PAGE 5-B

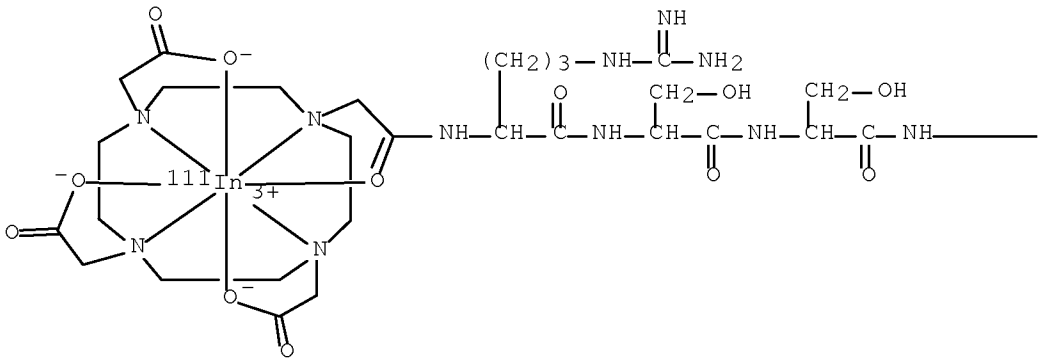


RN 728914-72-5 ZCAPLUS

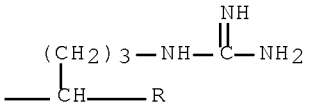
CN Indate(2-)-111In, [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-

κO]-L-arginyl-L-seryl-L-seryl-L-arginyl-L-tyrosyl-L-cysteinyl-L-cysteinyl-L-α-glutamyl-L-leucyl-L-cysteinyl-L-cysteinyl-L-asparaginyl-L-prolyl-L-alanyl-L-cysteinyl-L-threonylglycyl-L-cysteinyl-L-phenylalanine cyclic (6→11),(7→15),(10→18)-tris(disulfidato)(5-)]-, dihydrogen (9CI) (CA INDEX NAME)

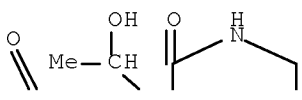
PAGE 1-A



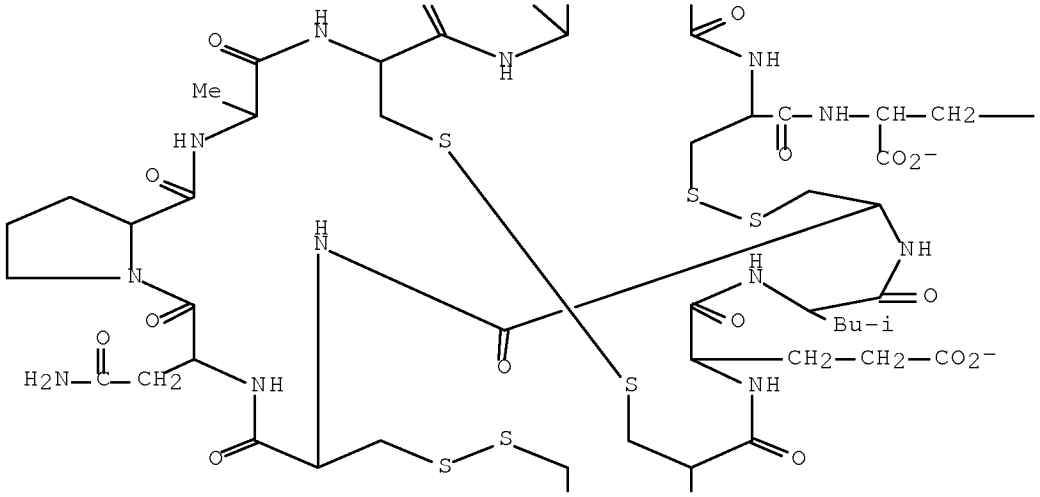
PAGE 1-B



PAGE 2-A



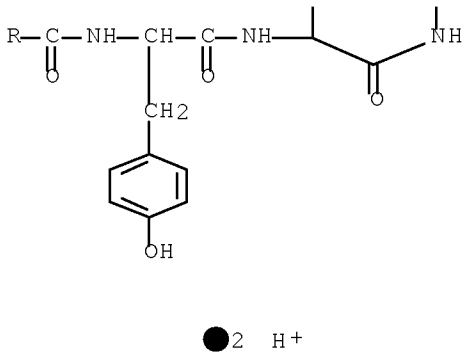
PAGE 3-A



PAGE 3-B

—Ph

PAGE 4-A



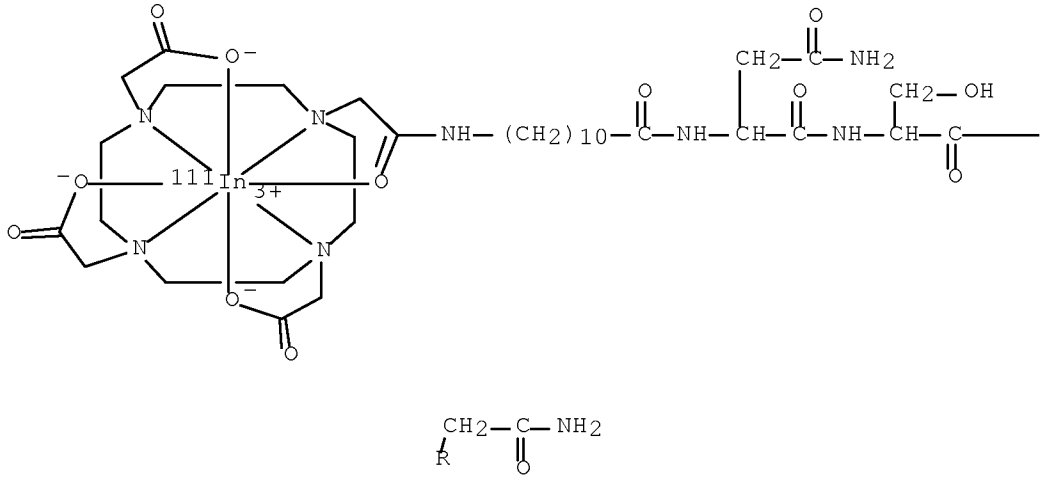
●2 H+

RN 728914-74-7 ZCAPLUS

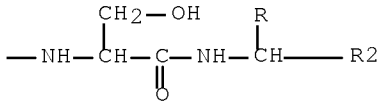
CN Indate(2-)-111In, [N2-[1-oxo-11-[[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]

acetyl-κO]amino]undecyl]-L-asparaginyl-L-seryl-L-seryl-L-asparaginyl-L-tyrosyl-L-cysteinyl-L-cysteinyl-L-α-glutamyl-L-leucyl-L-cysteinyl-L-cysteinyl-L-asparaginyl-L-prolyl-L-alanyl-L-cysteinyl-L-threonylglycyl-L-cysteinyl-L-phenylalanine cyclic (6→11),(7→15),(10→18)-tris(disulfidato)(5-)]-, dihydrogen (9CI) (CA INDEX NAME)

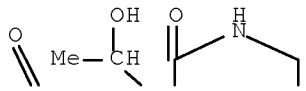
PAGE 1-A



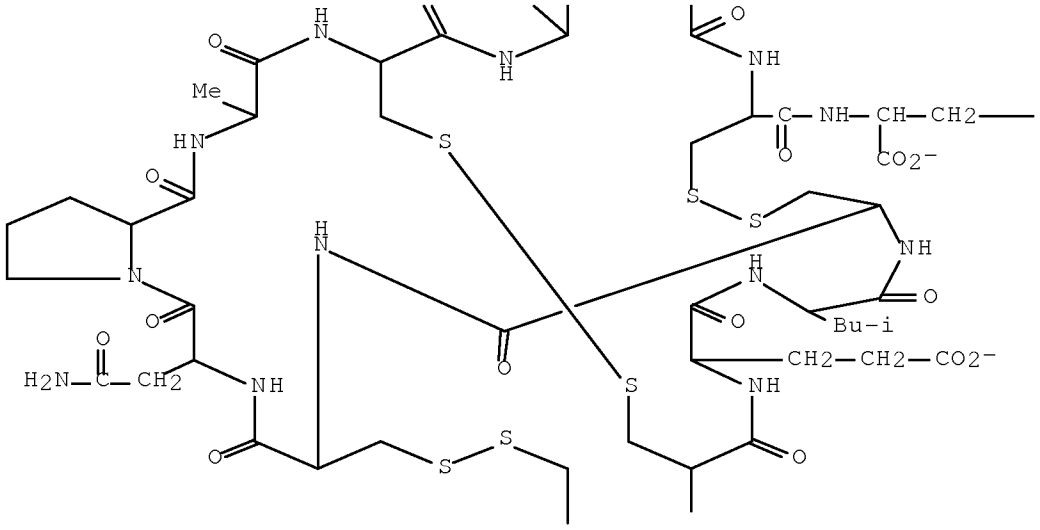
PAGE 1-B



PAGE 3-A

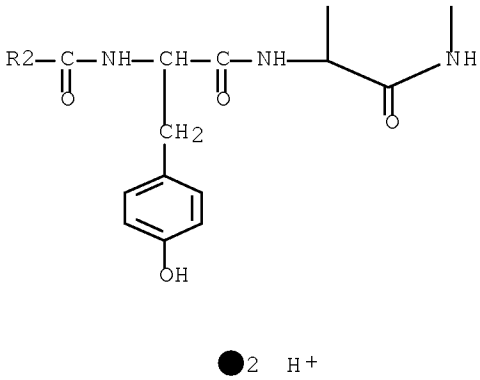


PAGE 4-A



PAGE 4-B

—Ph



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 11 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:261461 ZCAPLUS Full-text
DOCUMENT NUMBER: 142:70820
TITLE: Cellular Delivery of MRI Contrast Agents
AUTHOR(S): Allen, Matthew J.; MacRenaris, Keith W.; Venkatasubramanian, P. N.; Meade, Thomas J.
CORPORATE SOURCE: Dep. Chem., Biochem. and Mol. and Cell Biol., Neurobiol. and Physiol., and Radiol., Northwestern Univ., Evanston, IL, 60208, USA
SOURCE: Chemistry & Biology (2004), 11(3), 301-307
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Magnetic resonance imaging (MRI) is a powerful tool for acquiring images of opaque living animals with the benefit of tracking events over extended periods of time on the same specimen. Contrast agents are used to enhance regions, tissues, and cells that are magnetically similar but histol. distinct. A principal barrier to the development of MRI contrast agents for investigating biol. questions is the delivery of agents across cellular membranes. Here, we describe the synthesis and in vitro testing of Gd(III)-based MRI contrast agents containing varying length polyarginine oligomers capable of permeating cell membranes. We examine the effect of the length of oligomer on T1 enhancement and cellular uptake. Furthermore, the effect of incubation time, concentration, and cell type on uptake is explored. Toxicity and washout studies are performed in addition to MRI phantom studies.

CC 8-9 (Radiation Biochemistry)
IT 22541-18-0DP, Europium III, complexes with DOTA-polyarginine, biological studies 22541-19-1DP, Gadolinium(III), complexes with DOTA-polyarginine, biological studies 812644-18-1P 812644-19-2P 812644-20-5P 812644-21-6P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Gd(III)-based MRI contrast agents preparation and cellular uptake)
IT 811804-40-7P 811804-47-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(Gd(III)-based MRI contrast agents preparation and cellular uptake)

IT 22541-18-0DP, Europium III, complexes with DOTA-polyarginine, biological studies 22541-19-1DP, Gadolinium(III), complexes with DOTA-polyarginine, biological studies 812644-18-1P 812644-19-2P 812644-20-5P 812644-21-6P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Gd(III)-based MRI contrast agents preparation and cellular uptake)

RN 22541-18-0 ZCAPLUS
CN Europium, ion (Eu3+) (CA INDEX NAME)

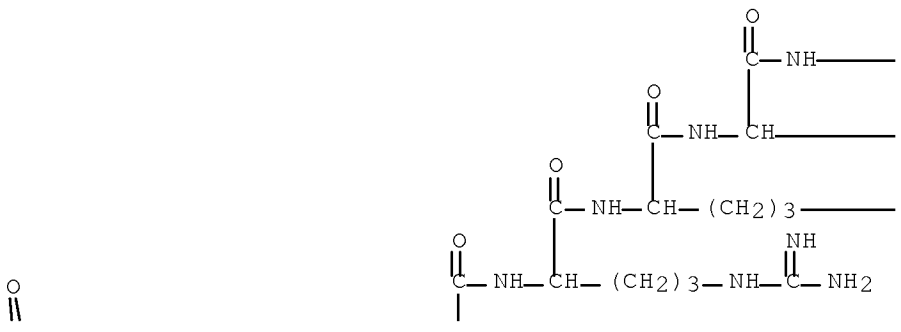
Eu^{3+}

RN 22541-19-1 ZCAPLUS
CN Gadolinium, ion (Gd3+) (CA INDEX NAME)

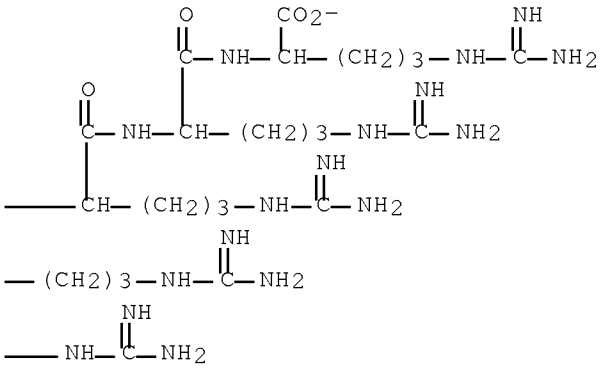
Gd^{3+}

RN 812644-18-1 ZCAPLUS
CN Gadolinate(1-), [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-argininato(4-)]-, hydrogen (9CI) (CA INDEX NAME)

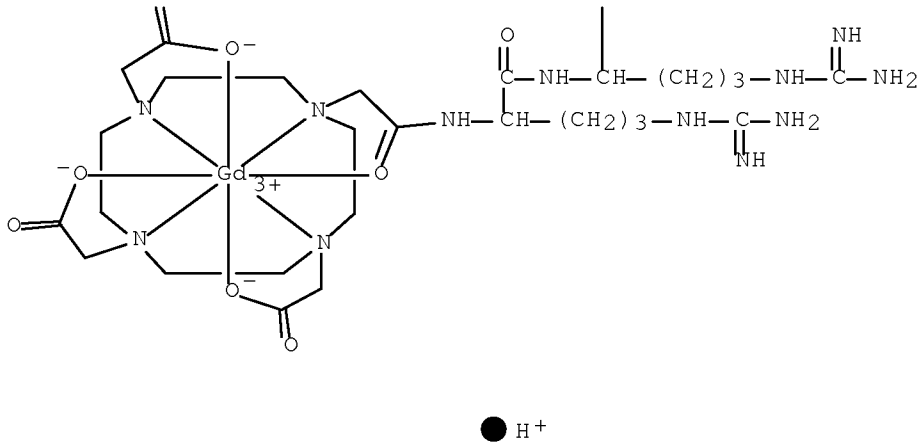
PAGE 1-A



PAGE 1-B



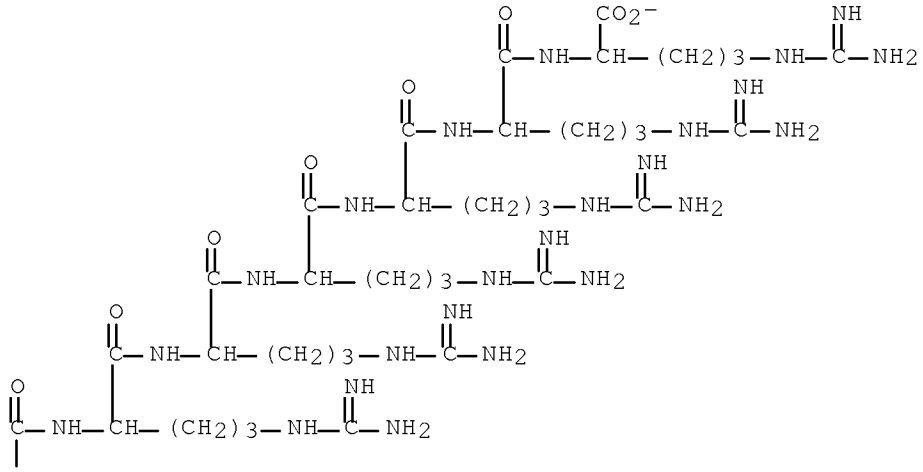
PAGE 2-A



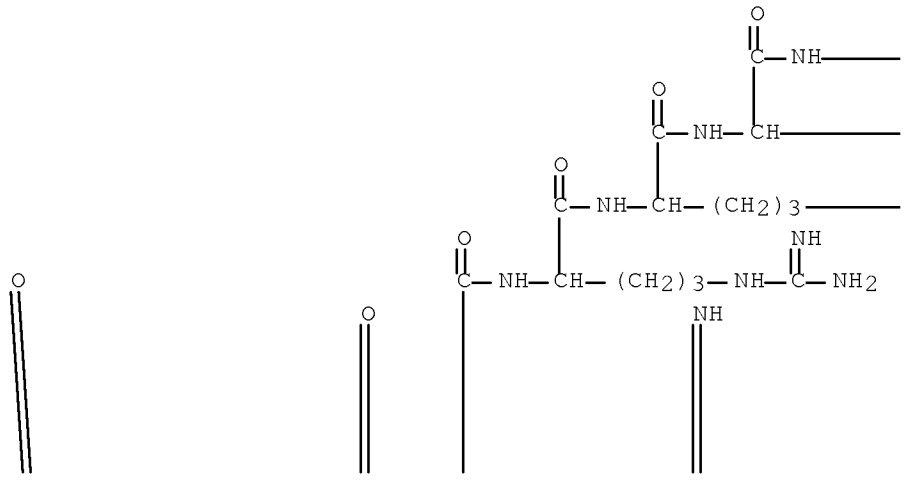
RN 812644-19-2 ZCAPLUS

CN Gadolinate(1-), [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-argininato(4-)]-, hydrogen (9CI) (CA INDEX NAME)

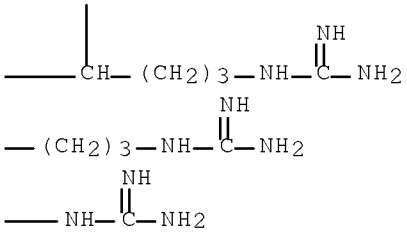
PAGE 1-B



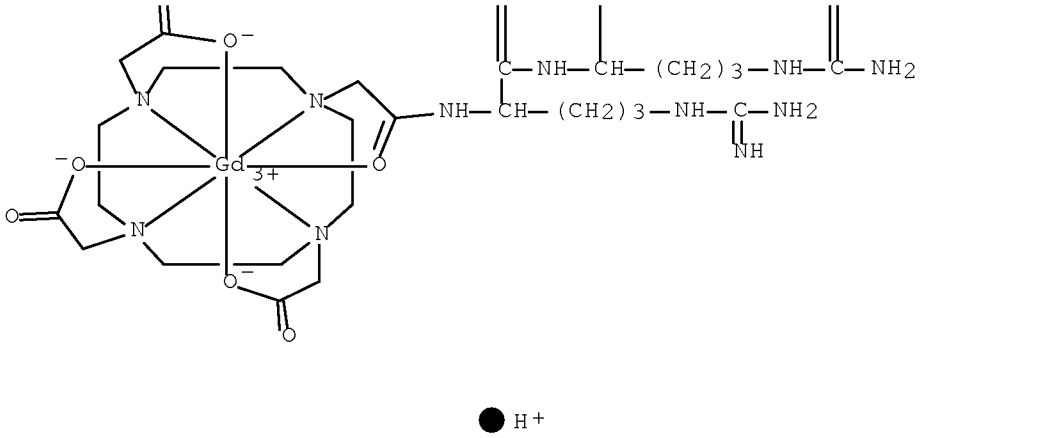
PAGE 2-A



PAGE 2-B



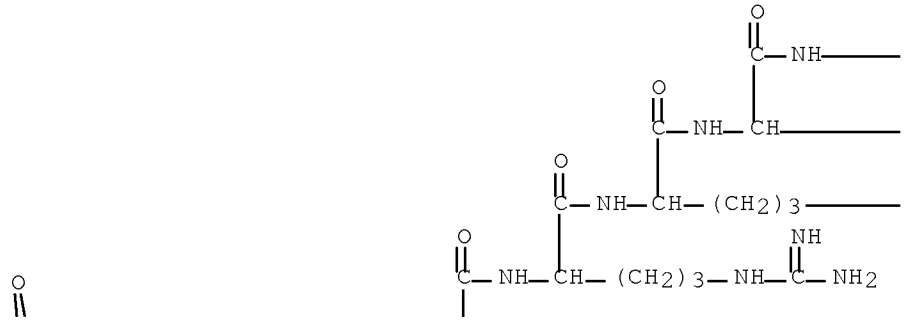
PAGE 3-A



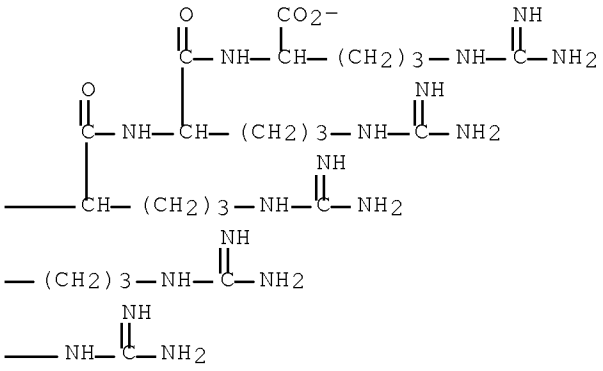
RN 812644-20-5 ZCAPLUS

CN Europate(1-), [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-argininato(4-)]-, hydrogen (9CI) (CA INDEX NAME)

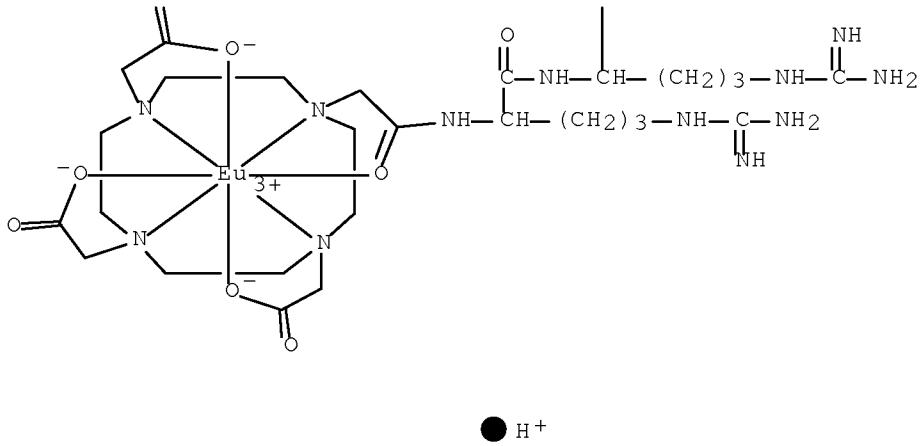
PAGE 1-A



PAGE 1-B



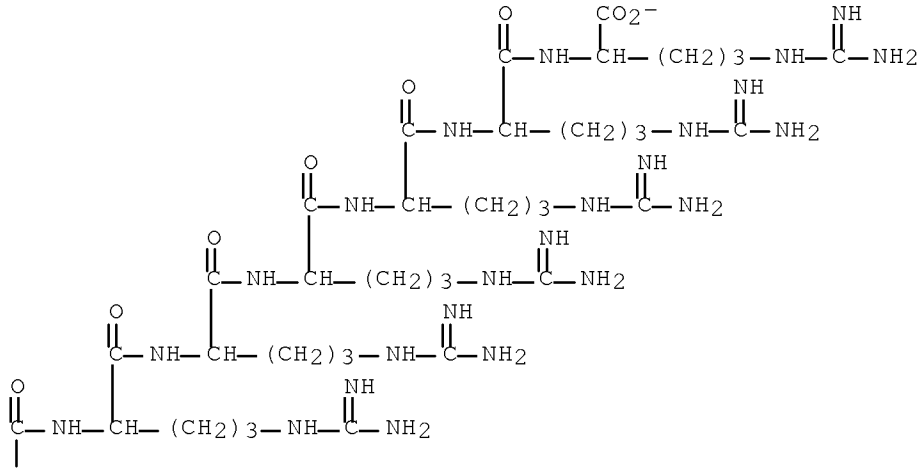
PAGE 2-A



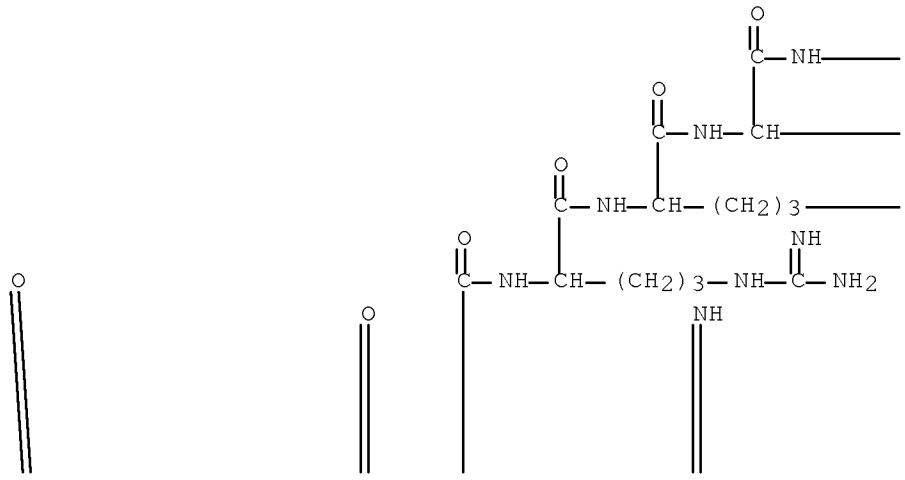
RN 812644-21-6 ZCAPLUS

CN Europate(1-), [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-argininato(4-)]-, hydrogen (9CI) (CA INDEX NAME)

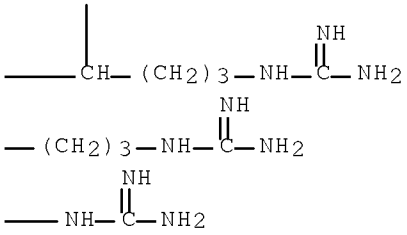
PAGE 1-B



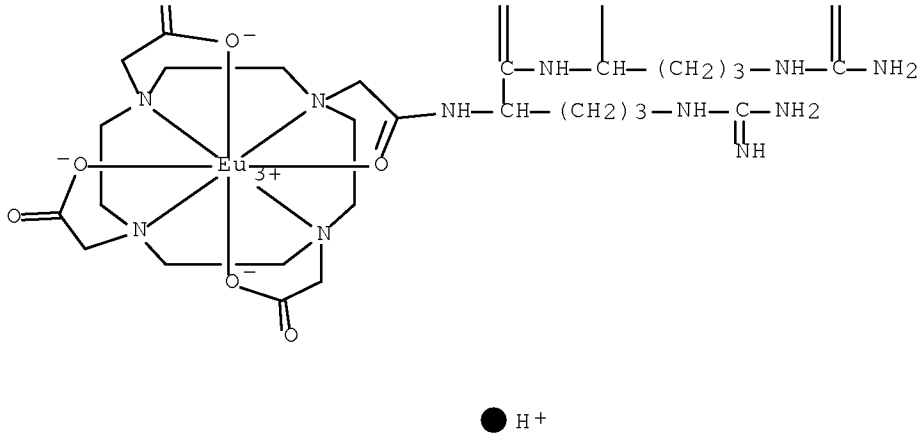
PAGE 2-A



PAGE 2-B



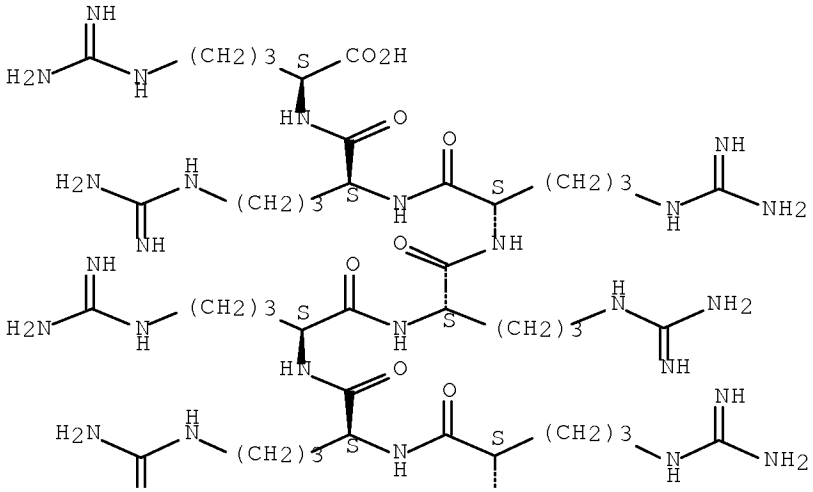
PAGE 3-A



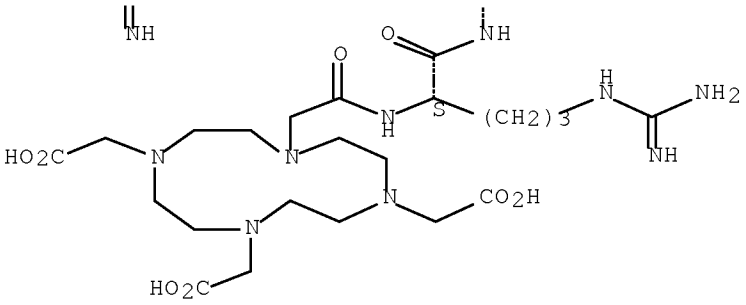
IT 811804-40-7P 811804-47-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(Gd(III)-based MRI contrast agents preparation and cellular uptake)
RN 811804-40-7 ZCAPLUS
CN L-Arginine, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



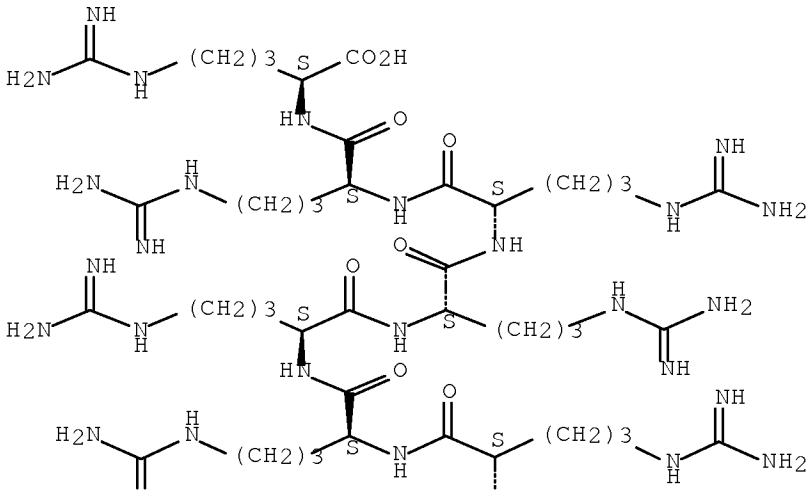
PAGE 2-A



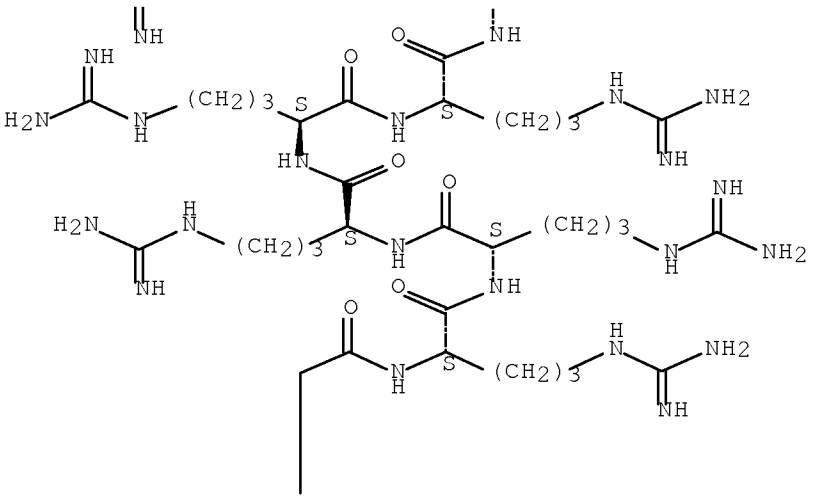
RN 811804-47-4 ZCAPLUS
CN L-Arginine, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

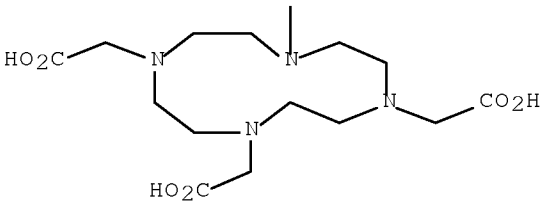
PAGE 1-A



PAGE 2-A



PAGE 3-A



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 12 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:750102 ZCAPLUS Full-text
DOCUMENT NUMBER: 139:214227
TITLE: A New Biotin Derivative-DOTA Conjugate as a Candidate for Pretargeted Diagnosis and Therapy of Tumors
AUTHOR(S): Sabatino, Giuseppina; Chinol, Marco; Paganelli, Giovanni; Papi, Stefano; Chelli, Mario; Leone, Giuseppe; Papini, Anna Maria; De Luca, Angelo; Ginanneschi, Mauro
CORPORATE SOURCE: Dep. of Org. Chem. "Ugo Schiff", CNR-ICCOM, Polo Scientifico, Univ. of Florence, Sesto Fiorentino, I-50019, Italy
SOURCE: Journal of Medicinal Chemistry (2003), 46(14), 3170-3173
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:214227

AB The synthesis of a new biotin derivative, the (CO) reduced N-aminohexyl biotinamido derivative, designed to be serum biotinidase resistant, and its conjugation to the chelator DOTA through an amide bond at one of the four carboxymethyl chains are described. The 90Y-labeled conjugate was able to bind avidin at different Av/conjugate molar ratios with good results. The preclin. The preclin. results indicate that this new biotin-DOTA conjugate is a good candidate for pretargeted diagnosis and therapy of tumors.

CC 26-8 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

ST aminohexyl biotinamido biotin deriv prepn; biotin DOTA conjugate prepn; stability avidin binding biotin DOTA conjugate; pretargeted diagnosis tumor therapy biotin DOTA conjugate prepn

IT Antitumor agents
Diagnostic agents
(preparation of a biotin-DOTA conjugate and evaluation of its serum stability and avidin binding properties as a candidate for pretargeted diagnosis and potential tumor therapy)

IT Avidins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of a biotin-DOTA conjugate and evaluation of its serum stability and avidin binding properties as a candidate for pretargeted diagnosis and potential tumor therapy)

IT 451478-45-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a biotin-DOTA conjugate and evaluation of its serum stability and avidin binding properties as a candidate for pretargeted diagnosis and potential tumor therapy)

IT 586962-90-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of a biotin-DOTA conjugate and evaluation of its serum stability and avidin binding properties as a candidate for pretargeted diagnosis and potential tumor therapy)

IT 58-85-5 51857-17-1 60239-18-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of a biotin-DOTA conjugate and evaluation of its serum stability and avidin binding properties as a candidate for pretargeted diagnosis and potential tumor therapy)

IT 65953-56-2P 153162-70-0P 451478-44-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a biotin-DOTA conjugate and evaluation of its serum stability and avidin binding properties as a candidate for pretargeted diagnosis and potential tumor therapy)

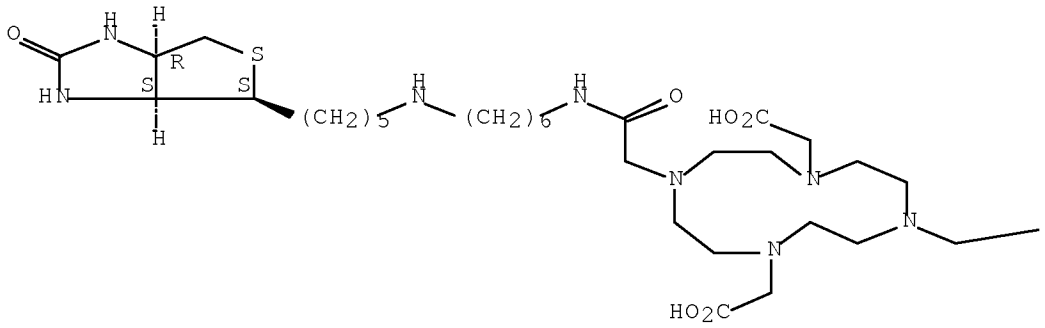
IT 451478-45-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a biotin-DOTA conjugate and evaluation of its serum stability and avidin binding properties as a candidate for pretargeted diagnosis and potential tumor therapy)

RN 451478-45-8 ZCAPLUS

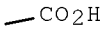
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]pentyl]amino]hexyl]amino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

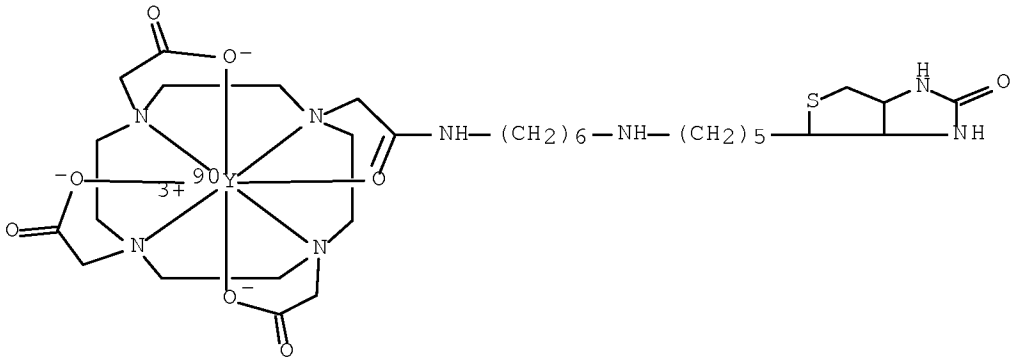
PAGE 1-A



PAGE 1-B



IT 586962-90-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of a biotin-DOTA conjugate and evaluation of its serum stability and avidin binding properties as a candidate for pretargeted diagnosis and potential tumor therapy)
RN 586962-90-5 ZCAPLUS
CN Yttrium-90Y, [10-[2-[[6-[[5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)pentyl]amino]hexyl]amino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,.kappa.N10,κO1,κo4,κO7]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 13 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:726127 ZCAPLUS Full-text
DOCUMENT NUMBER: 140:299530
TITLE: Synthesis and visualization of a membrane-permeable MRI contrast agent
AUTHOR(S): Allen, Matthew J.; Meade, Thomas J.
CORPORATE SOURCE: Division of Biology and the Beckman Institute, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: JBIC, Journal of Biological Inorganic Chemistry (2003), 8(7), 746-750
CODEN: JJBCFA; ISSN: 0949-8257
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The study of in vivo developmental events has undergone significant advances with the advent of biol. mol. imaging techniques such as computer enhanced light microscopy imaging, positron emission tomog. (PET), micro-CT, and magnetic resonance imaging (MRI). MRI has proven to be a particularly powerful tool in clin. and biol. settings. Images can be acquired of opaque living animals, with the benefit of tracking events of extended periods of time on the same specimen. Contrast agents are routinely used to enhance regions, tissues, and cells that are magnetically similar but histol. distinct. A principal barrier to the development of MR contrast agents for investigating developmental biol. questions is the ability to deliver the agent across cellular membranes. As part of our research, we are investigating a number of small mols. that facilitate transport of charged and uncharged species across cell membranes. Here we describe the synthesis and testing of a Gd(III)-based MR contrast agent conjugated to polyarginine that is able to permeate cell membranes. We confirmed cellular uptake of the agent using two-photon laser microscopy to visualize a Eu(III) derivative of the contrast agent in cell culture, and verified this uptake by T1 anal. of the Gd(III) agent in cells.

CC 8-9 (Radiation Biochemistry)
IT 112188-16-6P 137184-55-5P
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of Gd(III)-based membrane-permeable MRI contrast agent)
IT 676553-18-7P 676553-19-8P
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic

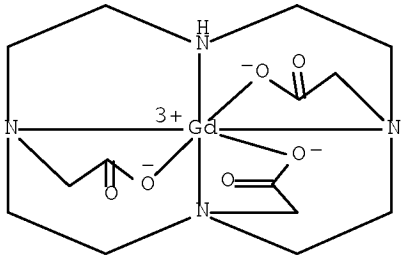
use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of Gd(III)-based membrane-permeable MRI contrast agent)

IT 676544-84-6P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of Gd(III)-based membrane-permeable MRI contrast agent)

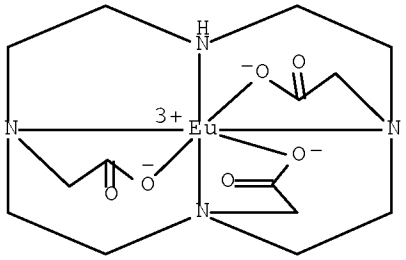
IT 7087-68-5, Diisopropylethylamine 91000-69-0D, L-Arginine, N2-[(9H-fluoren-9-ylmethoxy)carbonyl]-, resin-bound 137076-54-1, DOTA tri(tert-butyl) ester 148893-10-1, HATU 676544-85-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of Gd(III)-based membrane-permeable MRI contrast agent)

IT 112188-16-6P 137184-55-5P
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of Gd(III)-based membrane-permeable MRI contrast agent)

RN 112188-16-6 ZCAPLUS
CN Gadolinium, [1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-
(9CI) (CA INDEX NAME)



RN 137184-55-5 ZCAPLUS
CN Europium, [1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-
(9CI) (CA INDEX NAME)

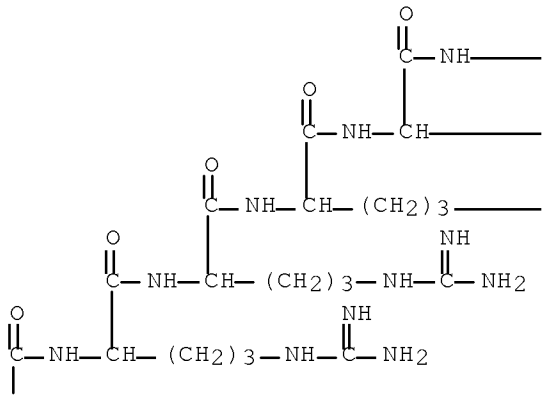


IT 676553-18-7P 676553-19-8P
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of Gd(III)-based membrane-permeable MRI contrast agent)

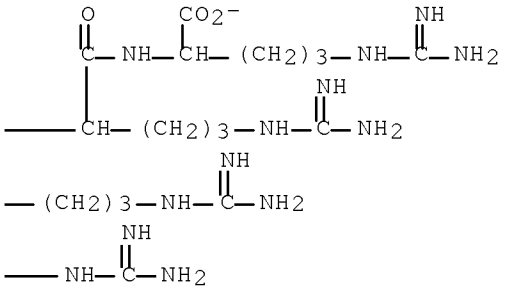
RN 676553-18-7 ZCAPLUS

CN Gadolinate(1-), [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl]-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-argininato(4-)]-, hydrogen (9CI) (CA INDEX NAME)

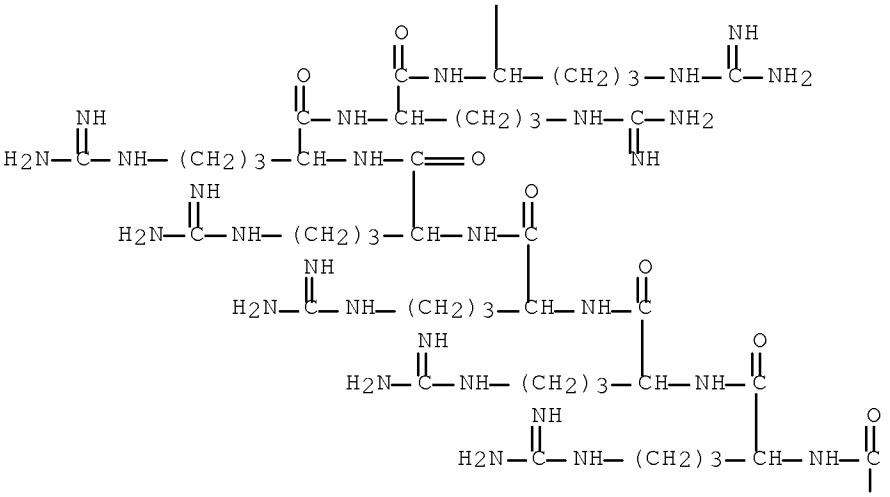
PAGE 1-A



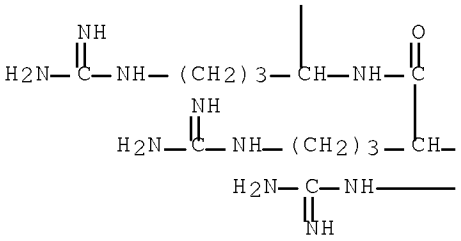
PAGE 1-B



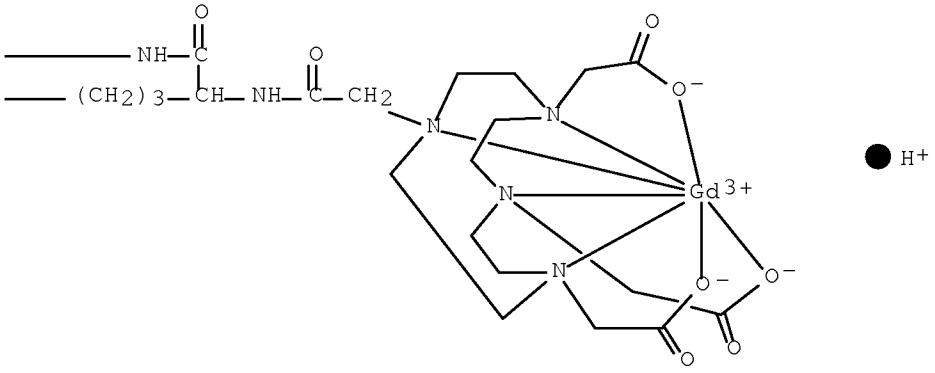
PAGE 2-A



PAGE 3-A



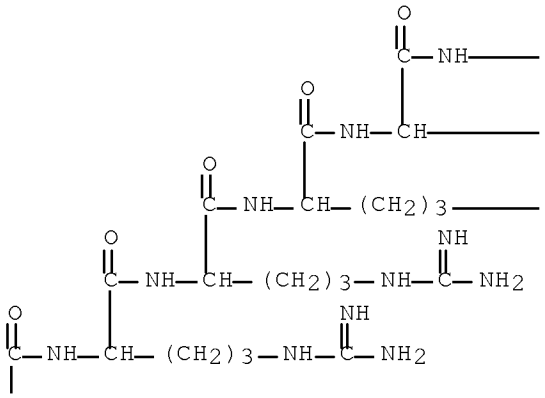
PAGE 3-B



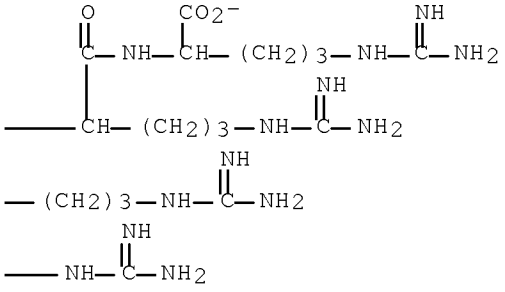
RN 676553-19-8 ZCAPLUS

CN Europate(1-), [N2-[[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl]-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-argininato(4-)]-, hydrogen (9CI) (CA INDEX NAME)

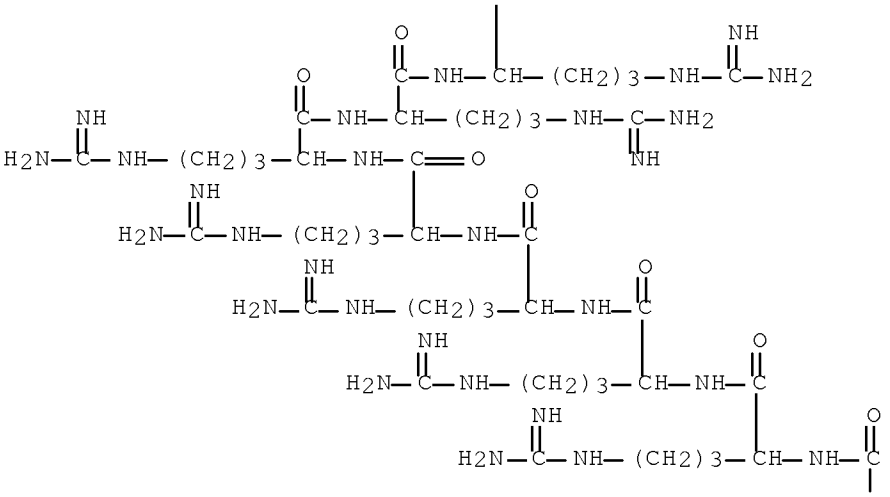
PAGE 1-A



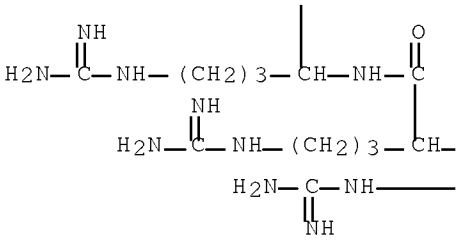
PAGE 1-B



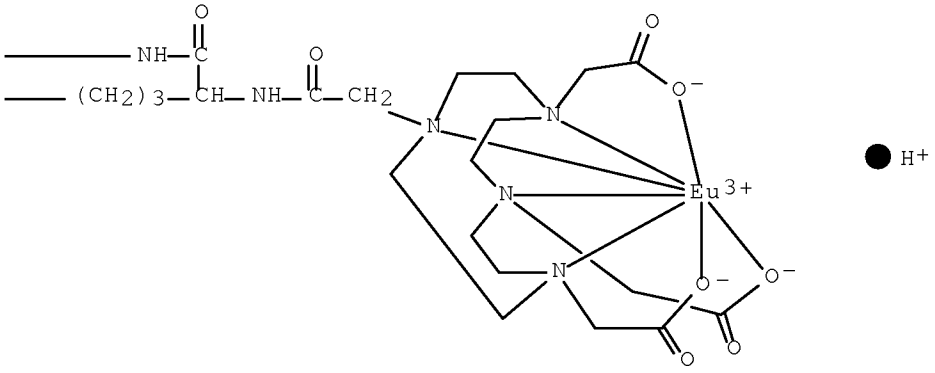
PAGE 2-A



PAGE 3-A



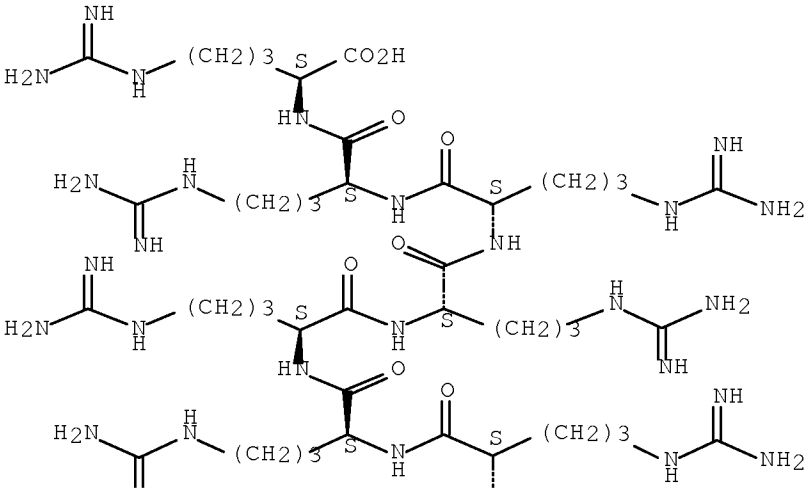
PAGE 3-B



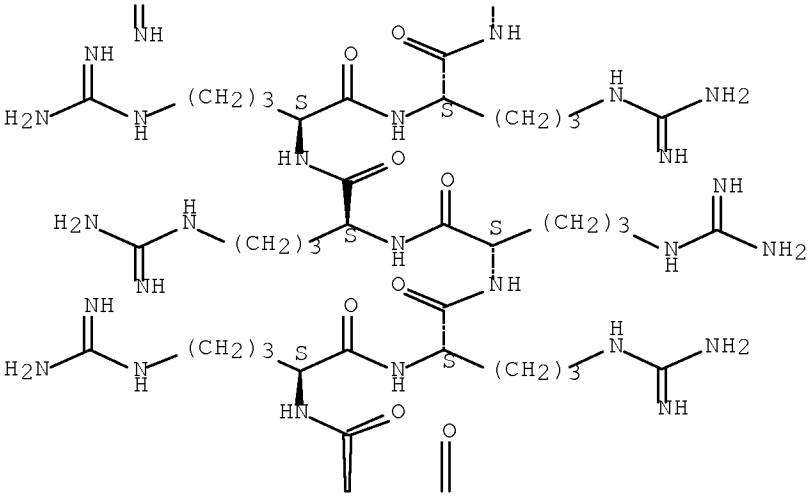
IT 676544-84-6P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of Gd(III)-based membrane-permeable MRI contrast agent)
RN 676544-84-6 ZCAPLUS
CN L-Arginine, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

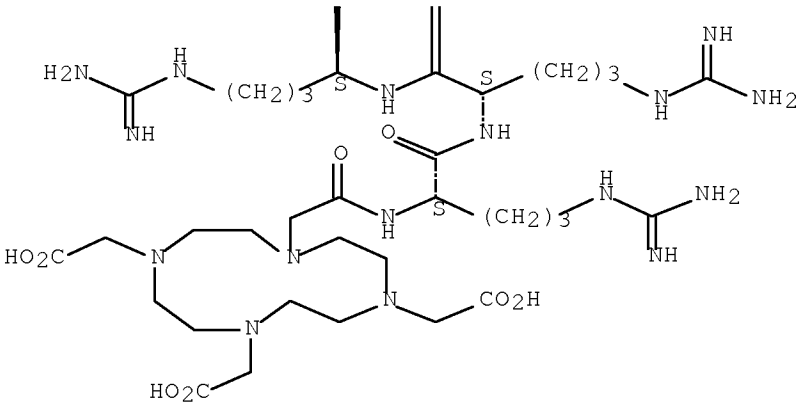
PAGE 1-A



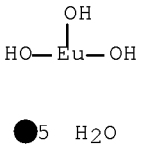
PAGE 2-A



PAGE 3-A



IT 676544-85-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of Gd(III)-based membrane-permeable MRI contrast agent)
RN 676544-85-7 ZCAPLUS
CN Europium hydroxide (Eu(OH)3), pentahydrate (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 14 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:71732 ZCAPLUS Full-text
DOCUMENT NUMBER: 138:122864
TITLE: Preparation of vitronectin receptor antagonist pharmaceuticals for use in the diagnosis and treatment of cancer
INVENTOR(S): Harris, Thomas D.; Barrett, John A.; Carpenter, Alan P., Jr.; Rajopadhye, Milind
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 146 pp., Cont.-in-part of U.S. Ser. No. 465,300.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6511649	B1	20030128	US 2000-599364	20000621

US 6322770	B1	20011127	US 1999-281207		19990330
US 2002015680	A1	20020207	US 1999-281209		19990330
US 6524553	B2	20030225			
US 6548663	B1	20030415	US 1999-281050		19990330
US 2002182147	A1	20021205	US 1999-465300		19991217
US 6511648	B2	20030128			
US 2002041878	A1	20020411	US 2001-948807		20010907
US 6683163	B2	20040127			
US 2002061909	A1	20020523	US 2001-948390		20010907
US 6689337	B2	20040210			
US 2003232053	A1	20031218	US 2001-947783		20010907
US 6743412	B2	20040601			
US 2003124120	A1	20030703	US 2002-269252		20021011
US 2003113336	A1	20030619	US 2002-281015		20021026
US 7018611	B2	20060328			
US 2003149262	A1	20030807	US 2002-306054		20021126
PRIORITY APPLN. INFO.:			US 1998-112732P	P	19981218
			US 1999-465300	A2	19991217
			US 1998-80150P	P	19980331
			US 1998-112715P	P	19981218
			US 1998-112829P	P	19981218
			US 1998-112831P	P	19981218
			US 1999-281050	A3	19990330
			US 1999-281209	A3	19990330
			US 2000-599364	A3	20000621

OTHER SOURCE(S): MARPAT 138:122864

AB Compds. (Q)d-Ln-Ch and (Q)d-Ln-(Ch)d' [Q is a residue having a quinolone-type moiety; Ln is a linking group; Ch is a metal-bonding unit; d = 1-10; d' = 1-100] and pharmaceutical compns. containing them were prepared for the treatment of cancer in combination therapy. The pharmaceuticals are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. The imageable moiety is a gamma ray or positron emitting radioisotope, a magnetic resonance imaging contrast agent, an X-ray contrast agent, or an ultrasound contrast agent. Thus, 2-[[[4-[4-[[[3-[2-[2-[3-[[6-[[1-aza-2-(2-sulfophenyl)vinyl]amino]-3-pyridyl]carbonylamino]propoxy]ethoxy]ethoxy]propyl]amino]sulfonyl]phenyl]phenyl]sulfonyl]amino]-3-[[7-[(imidazol-2-ylamino)methyl]-1-methyl-4-oxo-3-hydroquinolyl]carbonylamino]propanoic acid (claimed compound) was prepared

IC ICM A61K051-00
ICS A61M036-14

INCL 424001690; 424001110; 424001650; 424009100; 424009400; 424009500; 530331000

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 8, 27, 28, 63, 78

IT Angiogenesis
Antirheumatic agents
Antitumor agents
Human
Imaging agents
Radiopharmaceuticals
(preparation of peptide- and tetraazadodecane-containing quinolones and their
radioactive metal complexes for diagnosis and treatment of cancer)

IT 5704-04-1DP, Tricine, technetium-99 complexes 10098-91-6DP, complexes with vitronectin receptor binding conjugates, preparation 14133-76-7DP, complexes with vitronectin receptor binding conjugates, preparation 14265-75-9DP, complexes with vitronectin receptor binding conjugates, preparation 15750-15-9DP, complexes with vitronectin receptor binding

conjugates, preparation 63995-70-0DP, TPPTS, technetium-99 complexes
277315-51-2P 277315-52-3P 277315-53-4P 277315-55-6P 277315-56-7P
277315-57-8P 277315-58-9P 277315-59-0P 277315-60-3P 277315-61-4P
277315-62-5P 277315-63-6P 277315-64-7P 277315-65-8P 277315-67-0P
277315-68-1P 277315-69-2P 277315-70-5P 277315-72-7P
277315-74-9P 277315-75-0P 277315-76-1P 277315-77-2P
277315-78-3P 277315-79-4P 277315-80-7P 277315-81-8DP, technetium-99
complexes 277316-60-6P 277316-61-7P 277316-62-8P 277316-63-9P
277316-64-0P 277316-65-1P 277316-66-2P 277316-67-3P 277316-68-4P
277316-69-5P 278172-91-1P 278172-92-2P 278172-93-3P 278172-94-4P
278172-95-5P 278172-96-6P 278172-97-7P 278172-98-8P 278172-99-9P
278173-00-5P 278173-01-6P 278173-02-7P 278173-03-8P
278173-04-9P 278173-05-0P 278173-06-1P 278173-07-2P
278173-08-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of peptide- and tetraazadodecane-containing quinolones and
their
radioactive metal complexes for diagnosis and treatment of cancer)

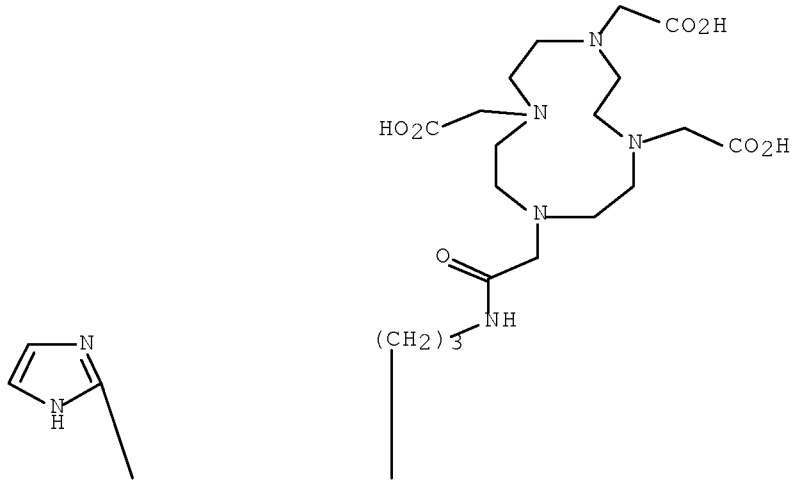
IT 40324-66-1P 57932-18-0P 137076-54-1P 192635-89-5P 220156-99-0P
250612-31-8P 277315-82-9P 277315-83-0P 277315-84-1P 277315-85-2P
277315-86-3P 277315-88-5P 277315-89-6P 277315-90-9P 277315-91-0P
277315-92-1P 277315-93-2P 277315-94-3P 277315-95-4P 277315-96-5P
277315-97-6P 277315-98-7P 277315-99-8P 277316-00-4P 277316-01-5P
277316-02-6P 277316-04-8P 277316-06-0P 277316-08-2P 277316-09-3P
277316-10-6P 277316-12-8P 277316-13-9P 277316-15-1P 277316-16-2P
277316-17-3P 277316-18-4P 277316-19-5P 277316-20-8P 277316-24-2P
277316-27-5P 277316-28-6P 277316-29-7P 277316-30-0P 277316-31-1P
277316-32-2P 277316-33-3P 277316-34-4P 277316-36-6P 277316-37-7P
277316-39-9P 277316-40-2P 277316-41-3P 277316-42-4P 277316-43-5P
277316-44-6P 277316-45-7P 277316-47-9P 277316-48-0P
277316-50-4P 277316-52-6P 277316-53-7P 277316-54-8P 277316-56-0P
277316-58-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of peptide- and tetraazadodecane-containing quinolones and
their
radioactive metal complexes for diagnosis and treatment of cancer)

IT 277315-74-9P 277315-75-0P 278173-04-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of peptide- and tetraazadodecane-containing quinolones and
their
radioactive metal complexes for diagnosis and treatment of cancer)

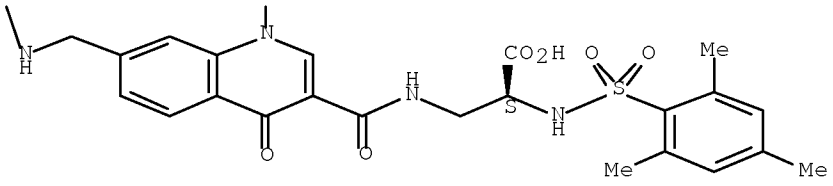
RN 277315-74-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[3-[[[(2S)-
2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-
7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-
oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



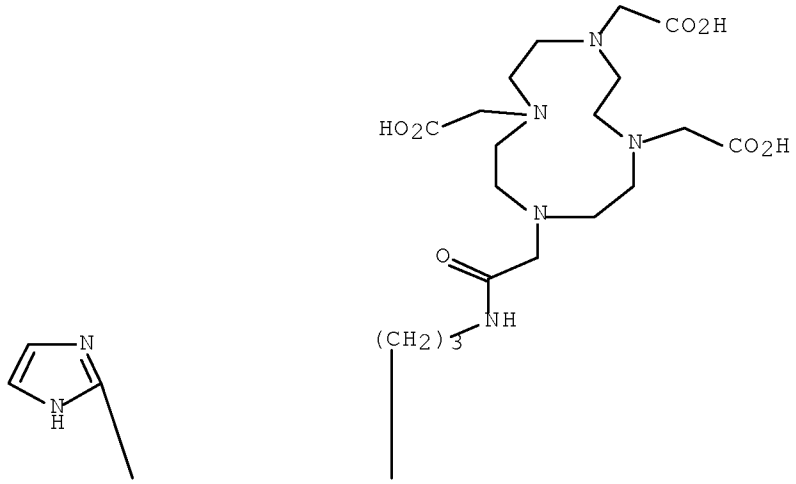
RN 277315-75-0 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-oxoethyl]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

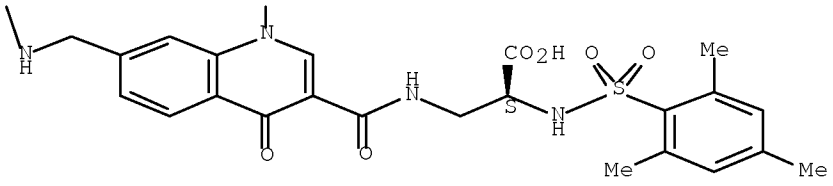
CRN 277315-74-9
CMF C45 H61 N11 O13 S

Absolute stereochemistry.

PAGE 1-A

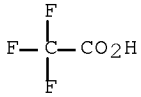


PAGE 2-A



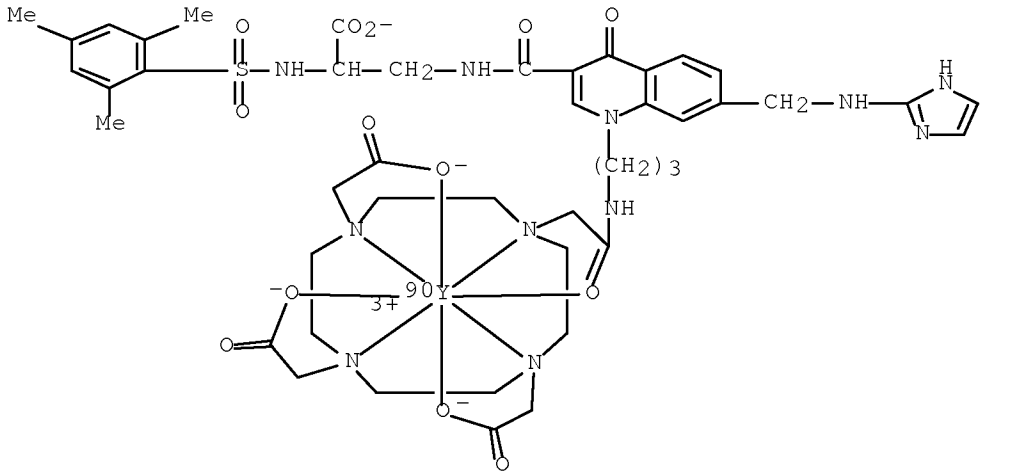
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 278173-04-9 ZCAPLUS
CN Yttrate(1-)-90Y, [10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(4-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-, hydrogen (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

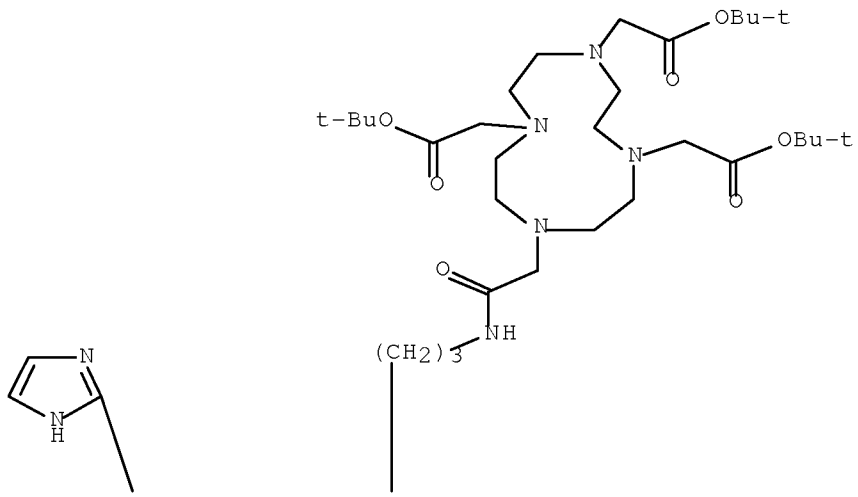
IT 277316-47-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide- and tetraazadodecane-containing quinolones and their
radioactive metal complexes for diagnosis and treatment of cancer)
RN 277316-47-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-oxoethyl]-, α,α',α''-tris(1,1-dimethylethyl) ester, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

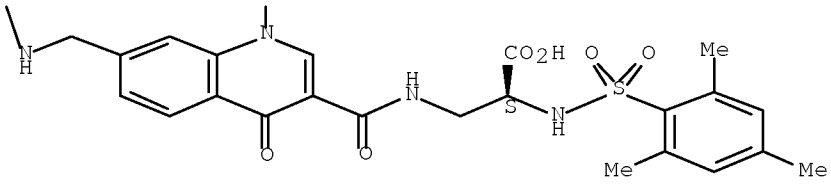
CRN 277316-46-8
CMF C57 H85 N11 O13 S

Absolute stereochemistry.

PAGE 1-A

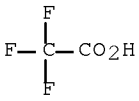


PAGE 2-A



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 143 THERE ARE 143 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 15 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:935440 ZCAPLUS Full-text
DOCUMENT NUMBER: 136:70082
TITLE: Vitronectin receptor antagonist pharmaceuticals for

use in combination therapy
INVENTOR(S): Harris, Thomas D.; Barrett, John A.; Carpenter, Alan P., Jr.; Rajopadhye, Milind
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA; Bristol-Myers Squibb Pharma. Company
SOURCE: PCT Int. Appl., 542 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001097848	A2	20011227	WO 2001-US19793		20010621
WO 2001097848	A3	20030313			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2412854	A1	20011227	CA 2001-2412854		20010621
EP 1307226	A2	20030507	EP 2001-952180		20010621
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004521066	T	20040715	JP 2002-503332		20010621
CN 1582166	A	20050216	CN 2001-814430		20010621
BR 2001011880	A	20060425	BR 2001-11880		20010621
NZ 522925	A	20060831	NZ 2001-522925		20010621
MX 2002PA12750	A	20040730	MX 2002-PA12750		20021218
IN 2007DN01157	A	20070427	IN 2007-DN1157		20070213
PRIORITY APPLN. INFO.:			US 2000-213210P	P	20000621
			WO 2001-US19793	W	20010621
			IN 2002-DN1168	A3	20021128

OTHER SOURCE(S): MARPAT 136:70082

AB Anticancer agents of the formulas (Q)d-Ln-Ch or (Q)d-Ln-(Ch)d (I) [Q is a residue having a quinolone-type moiety; Ln is a linking group; Ch is a metal-bonding unit; d = 1-10; d' = 1-100] and kits containing I are prepared for the treatment of cancer in combination therapy in a patient. I are comprised of a targeting moiety that binds to a receptor that is upregulated during angiogenesis, an optional linking group, and a therapeutically effective radioisotope or diagnostically effective imageable moiety. I may be used with radioisotopes; in addition, I may be used in conjunction with radio- and photosensitizers, ligands such as TPPTS or tricine, and reducing agents such as tin(II). The present invention provides novel compds. useful for the treatment of rheumatoid arthritis (no data).

IC ICM A61K041-00
ICS A61K051-04
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 8, 27, 28, 63, 78
IT Antitumor agents
(preparation of peptide- and tetraazadodecane-containing quinolones and their
radioactive metal complexes as anticancer agents)
IT 5704-04-1DP, Tricine, technetium-99 complexes 10098-91-6DP, complexes with vitronectin receptor binding conjugates, preparation 14133-76-7DP,

complexes with vitronectin receptor binding conjugates, preparation 14265-75-9DP, complexes with vitronectin receptor binding conjugates, preparation 15750-15-9DP, complexes with vitronectin receptor binding conjugates, preparation 63995-70-0DP, TPPTS, technetium-99 complexes 277315-51-2P 277315-52-3P 277315-53-4P 277315-55-6P 277315-56-7P 277315-57-8P 277315-58-9P 277315-59-0P 277315-60-3P 277315-61-4P 277315-62-5P 277315-63-6P 277315-64-7P 277315-65-8P 277315-67-0P 277315-68-1P 277315-69-2P 277315-70-5P 277315-72-7P 277315-74-9P 277315-75-0P 277315-76-1P 277315-77-2P 277315-78-3P 277315-79-4P 277315-80-7P 277315-81-8DP, technetium-99 complexes 277316-60-6P 277316-61-7P 277316-62-8P 277316-63-9P 277316-64-0P 277316-65-1P 277316-66-2P 277316-67-3P 277316-68-4P 277316-69-5P 278172-91-1P 278172-92-2P 278172-93-3P 278172-94-4P 278172-95-5P 278172-96-6P 278172-97-7P 278172-98-8P 278172-99-9P 278173-00-5P 278173-01-6P 278173-02-7P 278173-03-8P 278173-04-9P 278173-05-0P 278173-06-1P 278173-07-2P 278173-08-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide- and tetraazadodecane-containing quinolones and their radioactive metal complexes as anticancer agents)

IT 40324-66-1P 57932-18-0P 137076-54-1P 192635-89-5P 220156-99-0P 250612-31-8P 277315-82-9P 277315-83-0P 277315-84-1P 277315-85-2P 277315-86-3P 277315-88-5P 277315-89-6P 277315-90-9P 277315-91-0P 277315-92-1P 277315-93-2P 277315-94-3P 277315-95-4P 277315-96-5P 277315-97-6P 277315-98-7P 277315-99-8P 277316-00-4P 277316-01-5P 277316-02-6P 277316-04-8P 277316-06-0P 277316-08-2P 277316-09-3P 277316-10-6P 277316-12-8P 277316-13-9P 277316-15-1P 277316-16-2P 277316-17-3P 277316-18-4P 277316-19-5P 277316-20-8P 277316-24-2P 277316-27-5P 277316-28-6P 277316-29-7P 277316-30-0P 277316-31-1P 277316-32-2P 277316-33-3P 277316-34-4P 277316-36-6P 277316-37-7P 277316-39-9P 277316-40-2P 277316-41-3P 277316-42-4P 277316-43-5P 277316-44-6P 277316-45-7P 277316-47-9P 277316-48-0P 277316-50-4P 277316-52-6P 277316-53-7P 277316-54-8P 277316-56-0P 277316-58-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide- and tetraazadodecane-containing quinolones and their radioactive metal complexes as anticancer agents)

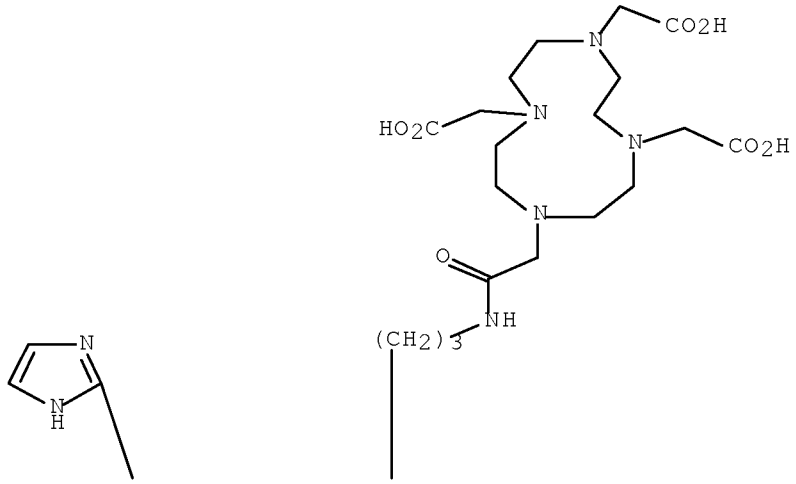
IT 277315-74-9P 277315-75-0P 278173-04-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide- and tetraazadodecane-containing quinolones and their radioactive metal complexes as anticancer agents)

RN 277315-74-9 ZCAPLUS

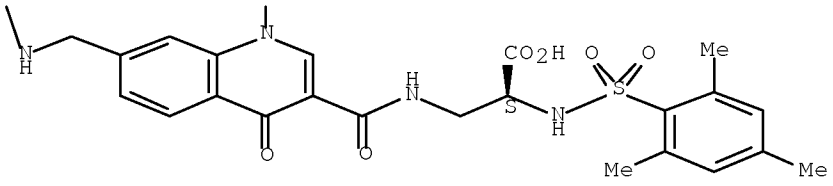
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



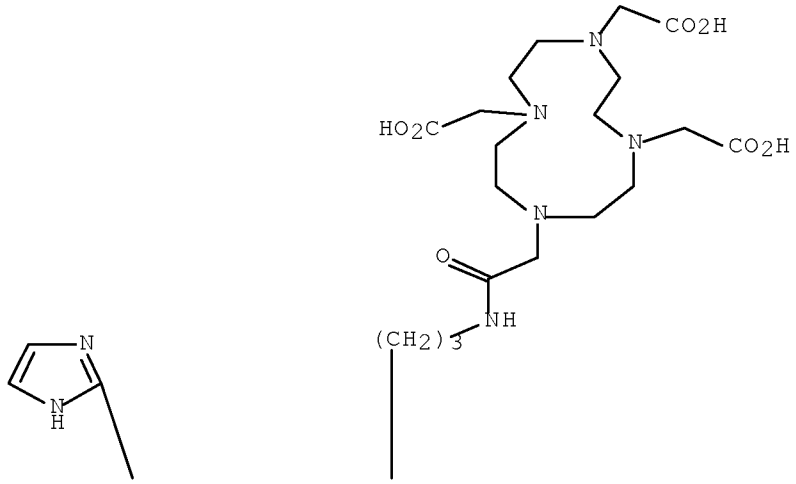
RN 277315-75-0 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-oxoethyl]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

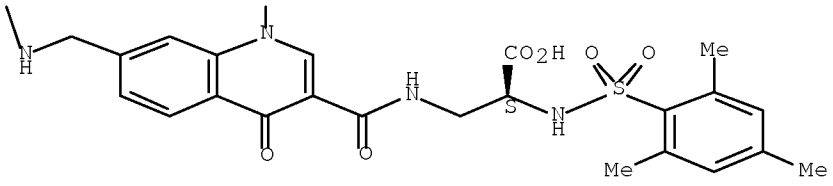
CRN 277315-74-9
CMF C45 H61 N11 O13 S

Absolute stereochemistry.

PAGE 1-A

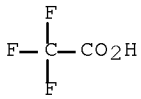


PAGE 2-A



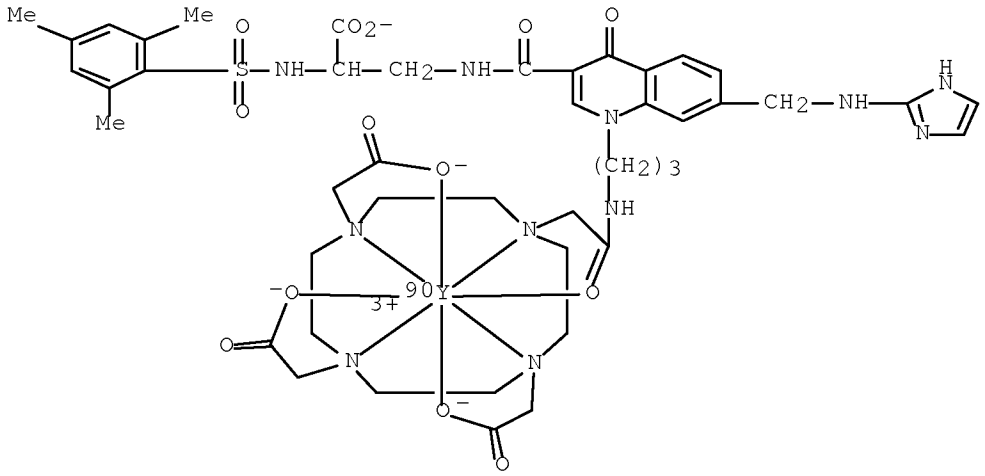
CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 278173-04-9 ZCAPLUS
CN Yttrate(1-)-90Y, [10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(4-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-, hydrogen (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

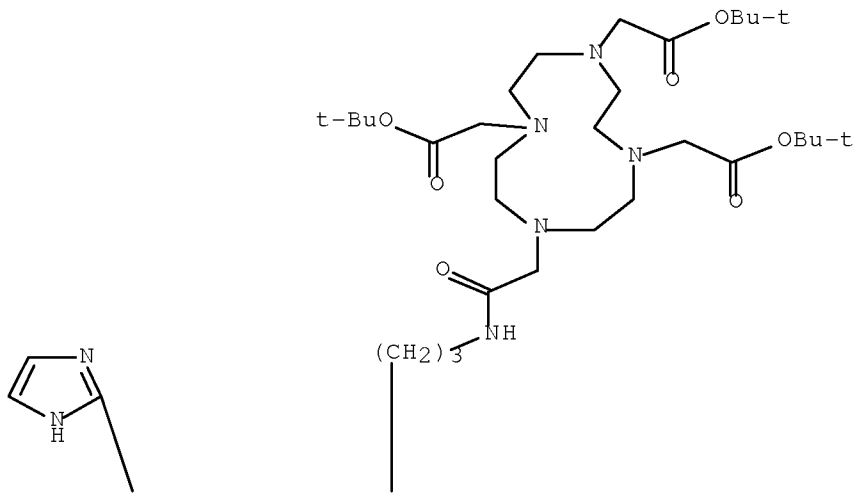
IT 277316-47-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide- and tetraazadodecane-containing quinolones and their
radioactive metal complexes as anticancer agents)
RN 277316-47-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-oxoethyl]-, α,α',α''-tris(1,1-dimethylethyl) ester, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

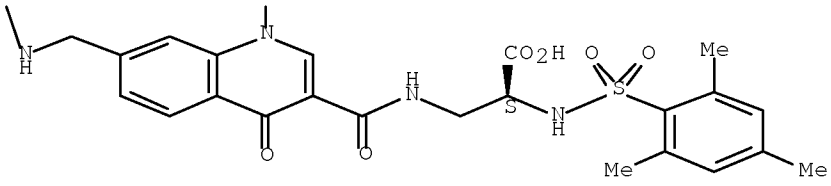
CRN 277316-46-8
CMF C57 H85 N11 O13 S

Absolute stereochemistry.

PAGE 1-A

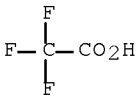


PAGE 2-A



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L79 ANSWER 16 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:661180 ZCAPLUS Full-text
DOCUMENT NUMBER: 133:249059
TITLE: Radionuclide conjugates with DOTA-biotin derivatives for diagnosis and therapy
INVENTOR(S): Griffiths, Gary L.; Hansen, Hans; Govindan, Serengulam V.

PATENT ASSIGNEE(S): Immunomedics, Inc., USA
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 486,166, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 19
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6120768	A	20000919	US 1997-990843	19971215
US 5736119	A	19980407	US 1995-409960	19950323
US 5922302	A	19990713	US 1995-440652	19950515
WO 9930745	A2	19990624	WO 1998-US26579	19981215
WO 9930745	A3	20000113		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9918258	A	19990705	AU 1999-18258	19981215

PRIORITY APPLN. INFO.:

US 1993-62662	B1	19930517
US 1995-409960	A2	19950323
US 1995-486166	B2	19950607
US 1996-688781	A2	19960731
US 1997-990843	A1	19971215
WO 1998-US26579	W	19981215

AB A radionuclide-chelator conjugate composition for detecting and/or treating lesions in a patient comprises pre-targeting the cell, tissue, or pathogen with a substrate, using a targeting protein that specifically binds a marker substance on the target cell, tissue, or pathogen and to which the substrate is directly or indirectly bound. Parenteral injection comprises a chelate conjugate of biotin, a chelator, and a chelatable detection or therapeutic agent, and allows the composition to accrete at the targeted cell, tissue, or pathogen. The chelate conjugate is purified by liquid chromatog. after chelate formation, or further comprises a blood transit-modifying linker or addend that is covalently bound within the chelate conjugate, or both. The detection or therapeutic agent of the invention are used to detect or treat cancer, infectious diseases, or cardiovascular diseases. Preparation of biotin-D-Phe-D-Lys-DOTA is presented.

IC ICM A61K039-395
INCL 424178100
CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 1, 15, 28, 34
ST DOTA biotin deriv chelator radionuclide conjugate; diagnosis therapy DOTA biotin deriv radionuclide; antitumor antiinfective cardiovascular agent radionuclide conjugate
IT Antitumor agents
(carcinoma; radionuclide conjugates with DOTA-biotin derivs. for diagnosis and therapy)
IT Antitumor agents
(glioma; radionuclide conjugates with DOTA-biotin derivs. for diagnosis and therapy)
IT Antitumor agents
(leukemia; radionuclide conjugates with DOTA-biotin derivs. for diagnosis and therapy)

IT Antitumor agents
(lymphoma; radionuclide conjugates with DOTA-biotin derivs. for diagnosis and therapy)
IT Antitumor agents
(melanoma; radionuclide conjugates with DOTA-biotin derivs. for diagnosis and therapy)
IT Antitumor agents
(myeloma; radionuclide conjugates with DOTA-biotin derivs. for diagnosis and therapy)
IT Antitumor agents
(neuroblastoma; radionuclide conjugates with DOTA-biotin derivs. for diagnosis and therapy)
IT Anti-infective agents
Antimicrobial agents
Antitumor agents
Cardiovascular agents
Parasiticides
(radionuclide conjugates with DOTA-biotin derivs. for diagnosis and therapy)
IT Antitumor agents
(sarcoma; radionuclide conjugates with DOTA-biotin derivs. for diagnosis and therapy)
IT 7440-54-2DP, Gadolinium, chelates with DOTA-biotin derivs., biological studies 10043-49-9DP, Gold 198, chelates with DOTA-biotin derivs., biological studies 10098-91-6DP, Yttrium 90, chelates with DOTA-biotin derivs., biological studies 13967-65-2DP, Holmium-166, chelates with DOTA-biotin derivs., biological studies 13968-53-1DP, Ruthenium 103, chelates with DOTA-biotin derivs., biological studies 13981-51-6DP, Mercury 197, chelates with DOTA-biotin derivs., biological studies 14119-09-6DP, Gallium 67, chelates with DOTA-biotin derivs., biological studies 14119-24-5DP, Osmium 191, chelates with DOTA-biotin derivs., biological studies 14133-76-7DP, Technetium 99, chelates with DOTA-biotin derivs., biological studies 14191-64-1DP, Praseodymium 142, chelates with DOTA-biotin derivs., biological studies 14265-75-9DP, Lutetium 177, chelates with DOTA-biotin derivs., biological studies 14265-85-1DP, Actinium 225, chelates with DOTA-biotin derivs., biological studies 14331-95-4DP, Ruthenium 105, chelates with DOTA-biotin derivs., biological studies 14378-26-8DP, Rhenium 188, chelates with DOTA-biotin derivs., biological studies 14391-11-8DP, Gold 199, chelates with DOTA-biotin derivs., biological studies 14391-19-6DP, Terbium 161, chelates with DOTA-biotin derivs., biological studies 14391-96-9DP, Scandium 47, chelates with DOTA-biotin derivs., biological studies 14687-25-3DP, Lead 203, chelates with DOTA-biotin derivs., biological studies 14885-78-0DP, Indium 113, chelates with DOTA-biotin derivs., biological studies 14913-49-6DP, Bismuth 212, chelates with DOTA-biotin derivs., biological studies 14913-89-4DP, chelates with DOTA-biotin derivs., biological studies 14914-68-2DP, Antimony 119, chelates with DOTA-biotin derivs., biological studies 14967-68-1DP, Palladium 103, chelates with DOTA-biotin derivs., biological studies 14981-64-7DP, Palladium 109, chelates with DOTA-biotin derivs., biological studies 14998-63-1DP, Rhenium 186, chelates with DOTA-biotin derivs., biological studies 15092-94-1DP, Lead 212, chelates with DOTA-biotin derivs., biological studies 15735-74-7DP, Platinum 197, chelates with DOTA-biotin derivs., biological studies 15750-15-9DP, Indium 111, chelates with DOTA-biotin derivs., biological studies 15756-62-4DP, Ruthenium 95, chelates with DOTA-biotin derivs., biological studies 15757-14-9DP, Gallium 68, chelates with DOTA-biotin derivs., biological studies 15757-86-5DP, Copper 67, chelates with DOTA-biotin derivs., biological studies 15758-35-7DP, Ruthenium 97, chelates with DOTA-biotin derivs., biological studies 15760-04-0DP, Silver 111, chelates with DOTA-biotin

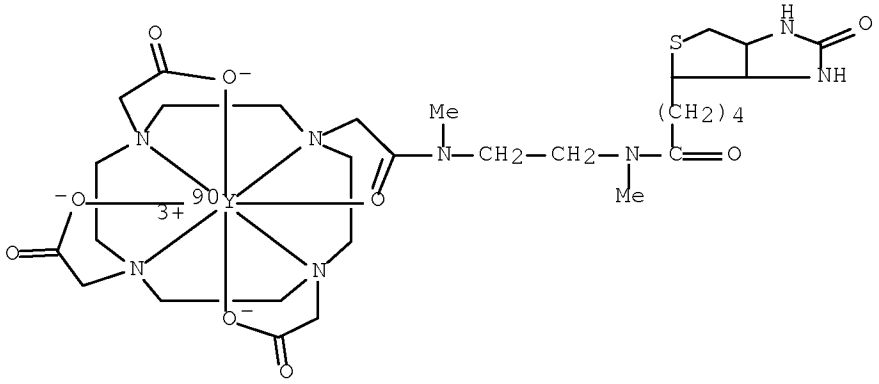
derivs., biological studies 15765-78-3DP, Rhenium 189, chelates with DOTA-biotin derivs., biological studies 15766-00-4DP, Samarium 153, chelates with DOTA-biotin derivs., biological studies 294638-18-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(radionuclide conjugates containing DOTA-biotin derivs. for diagnosis and therapy)

IT 170908-81-3P 192221-17-3P 192221-18-4P 192221-19-5P
245758-39-8P 294637-28-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radionuclide conjugates containing DOTA-biotin derivs. for diagnosis and therapy)

IT 294638-18-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(radionuclide conjugates containing DOTA-biotin derivs. for diagnosis and therapy)

RN 294638-18-9 ZCAPLUS

CN Yttrium-90Y, [10-[2-[[2-[[5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-1-oxopentyl]methylamino]ethyl]methylamino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-(9CI) (CA INDEX NAME)



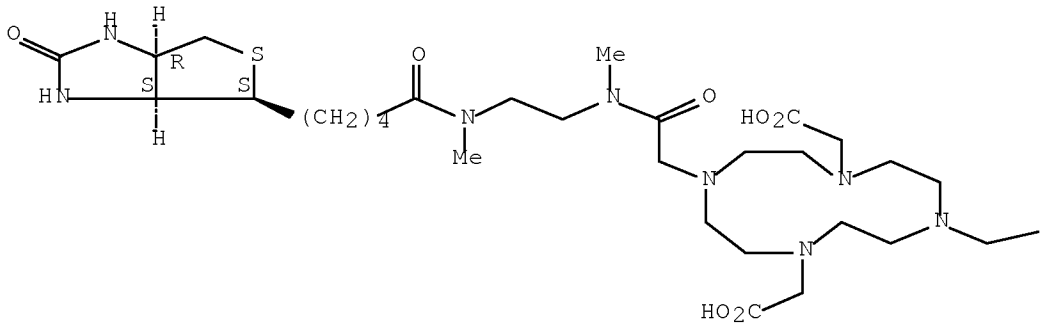
IT 245758-39-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radionuclide conjugates containing DOTA-biotin derivs. for diagnosis and therapy)

RN 245758-39-8 ZCAPLUS

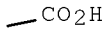
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]methylamino]ethyl]methylamino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 17 OF 17 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:420994 ZCAPLUS Full-text
DOCUMENT NUMBER: 133:59099
TITLE: Preparation of vitronectin receptor antagonist pharmaceuticals
INVENTOR(S): Harris, Thomas David; Rajodadhye, Milind
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 300 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035492	A2	20000622	WO 1999-US30315	19991217
WO 2000035492	A3	20010118		
W: AL, AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6322770	B1	20011127	US 1999-281207	19990330

US 2002015680	A1	20020207	US 1999-281209	19990330
US 6524553	B2	20030225		
US 6548663	B1	20030415	US 1999-281050	19990330
CA 2349501	A1	20000622	CA 1999-2349501	19991217
EP 1140204	A2	20011010	EP 1999-967443	19991217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9917079	A	20011030	BR 1999-17079	19991217
JP 2002532440	T	20021002	JP 2000-587811	19991217
AU 766822	B2	20031023	AU 2000-23716	19991217
NZ 511677	A	20031031	NZ 1999-511677	19991217
ZA 2001003675	A	20020607	ZA 2001-3675	20010507
IN 2001MN00576	A	20050304	IN 2001-MN576	20010522
MX 2001PA06151	A	20020311	MX 2001-PA6151	20010615
US 2003124120	A1	20030703	US 2002-269252	20021011
US 2003149262	A1	20030807	US 2002-306054	20021126
PRIORITY APPLN. INFO.:			US 1998-112732P	P 19981218
			US 1998-80150P	P 19980331
			US 1998-112715P	P 19981218
			US 1998-112829P	P 19981218
			US 1998-112831P	P 19981218
			US 1999-281050	A3 19990330
			US 1999-281209	A3 19990330
			WO 1999-US30315	W 19991217

OTHER SOURCE(S): MARPAT 133:59099

AB Compds. (Q)d-Ln-Ch (Q is a residue having a quinolone-type moiety , d = 1-10, Ln is a linking group, Ch is a metal-bonding unit) were prepared for use in the diagnosis and treatment of cancer, methods of imaging tumors in a patient, and methods of treating cancer in a patient. The present invention also provides novel compds. useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. Thus, [3-[1-[3-[3-[N-[3-[2-[N-(L-Asp-L-Asp)-3-aminopropoxy]ethoxy]ethoxy]propyl]carbamoyl]propanoylamino]propyl]-7-[(imidazol-2-ylamino)methyl]-4-oxo(3-hydroquinolyl)carbonylamino]-2- [[(2,4,6-trimethylphenyl)sulfonyl]amino]propanoic acid DOTA conjugate was prepared (claimed compound). Syntheses of radiopharmaceuticals, e.g., 99mTc(VnA)(tricine)(phosphine), where VnA represents the vitronectin receptor antagonist, are also described.

IC ICM A61K051-04

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 8, 27, 28, 63, 78

IT Angiogenesis
Antitumor agents
Atherosclerosis
Radiopharmaceuticals
(preparation of vitronectin receptor antagonist pharmaceuticals)

IT 40324-66-1P 57932-18-0P 137076-54-1P 192635-89-5P 220156-99-0P
250612-31-8P 277315-82-9P 277315-83-0P 277315-84-1P 277315-85-2P
277315-86-3P 277315-88-5P 277315-89-6P 277315-90-9P 277315-91-0P
277315-92-1P 277315-93-2P 277315-94-3P 277315-95-4P 277315-96-5P
277315-97-6P 277315-98-7P 277315-99-8P 277316-00-4P 277316-01-5P
277316-02-6P 277316-04-8P 277316-06-0P 277316-08-2P 277316-09-3P
277316-10-6P 277316-12-8P 277316-13-9P 277316-15-1P 277316-16-2P
277316-17-3P 277316-18-4P 277316-19-5P 277316-20-8P 277316-24-2P
277316-27-5P 277316-28-6P 277316-29-7P 277316-30-0P 277316-31-1P
277316-32-2P 277316-33-3P 277316-34-4P 277316-36-6P 277316-37-7P
277316-39-9P 277316-40-2P 277316-41-3P 277316-42-4P 277316-43-5P
277316-44-6P 277316-45-7P 277316-47-9P 277316-48-0P
277316-50-4P 277316-52-6P 277316-53-7P 277316-54-8P 277316-56-0P
277316-58-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of vitronectin receptor antagonist pharmaceuticals)

IT 5704-04-1DP, Tricine, technetium-99 complexes 10098-91-6DP, complexes with vitronectin receptor binding conjugates, preparation 14133-76-7DP, complexes with vitronectin receptor binding conjugates, preparation 14265-75-9DP, complexes with vitronectin receptor binding conjugates, preparation 15750-15-9DP, complexes with vitronectin receptor binding conjugates, preparation 63995-70-0DP, TPPTS, technetium-99 complexes 277315-51-2P 277315-52-3P 277315-53-4P 277315-55-6P 277315-56-7P 277315-57-8P 277315-58-9P 277315-59-0P 277315-60-3P 277315-61-4P 277315-62-5P 277315-63-6P 277315-64-7P 277315-65-8P 277315-67-0P 277315-68-1P 277315-69-2P 277315-70-5P 277315-72-7P 277315-74-9P 277315-75-0P 277315-76-1P 277315-77-2P 277315-78-3P 277315-79-4P 277315-80-7P 277315-81-8DP, technetium-99 complexes 277316-60-6P 277316-61-7P 277316-62-8P 277316-63-9P 277316-64-0P 277316-65-1P 277316-66-2P 277316-67-3P 277316-68-4P 277316-69-5P 277316-71-9DP, technetium-99 complexes 277316-72-0DP, technetium-99 complexes 277316-73-1DP, technetium-99 complexes 277316-74-2DP, technetium-99 complexes 277316-75-3DP, technetium-99 complexes 277316-76-4DP, technetium-99 complexes 278172-91-1P 278172-92-2P 278172-93-3P 278172-94-4P 278172-95-5P 278172-96-6P 278172-97-7P 278172-98-8P 278172-99-9P 278173-00-5P 278173-01-6P 278173-02-7P 278173-03-8P 278173-04-9P 278173-05-0P 278173-06-1P 278173-07-2P 278173-08-3P 278173-09-4DP, gadolinium-labeled
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of vitronectin receptor antagonist pharmaceuticals)

IT 277316-47-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of vitronectin receptor antagonist pharmaceuticals)

RN 277316-47-9 ZCAPLUS

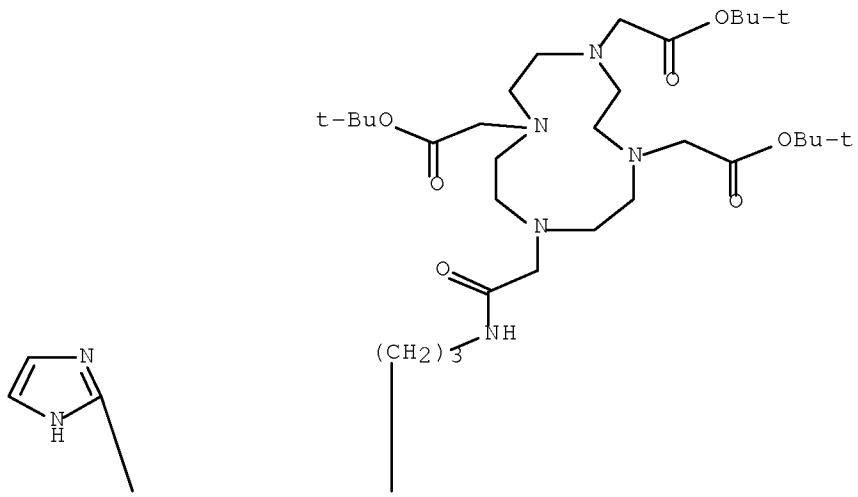
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-oxoethyl]-, α,α',α''-tris(1,1-dimethylethyl) ester, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

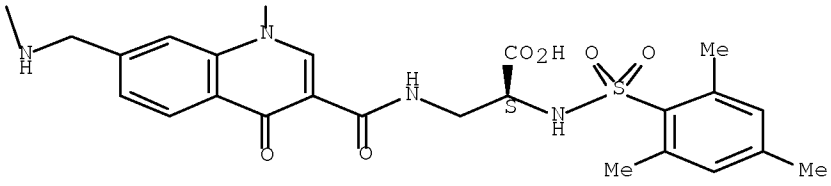
CRN 277316-46-8
CMF C57 H85 N11 O13 S

Absolute stereochemistry.

PAGE 1-A

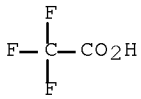


PAGE 2-A



CM 2

CRN 76-05-1
CMF C2 H F3 O2

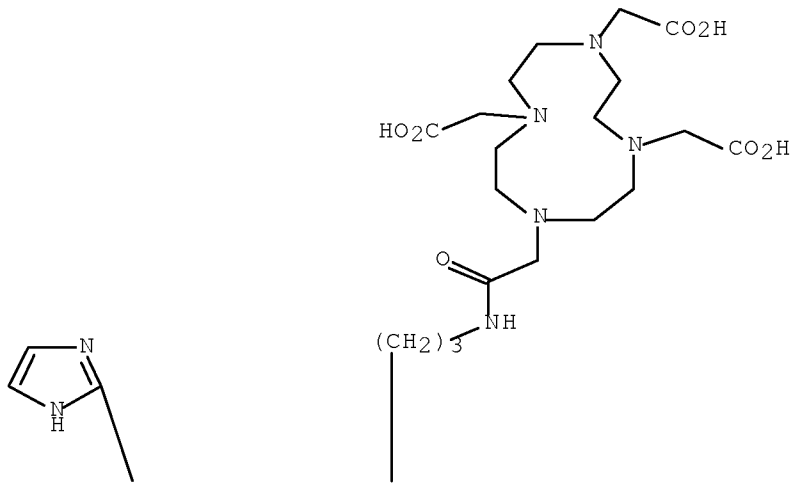


IT 277315-74-9P 277315-75-0P 278173-04-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of vitronectin receptor antagonist pharmaceuticals)
RN 277315-74-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-

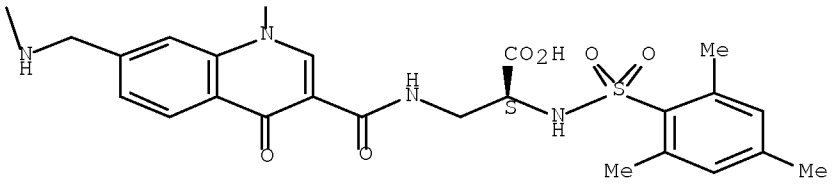
oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



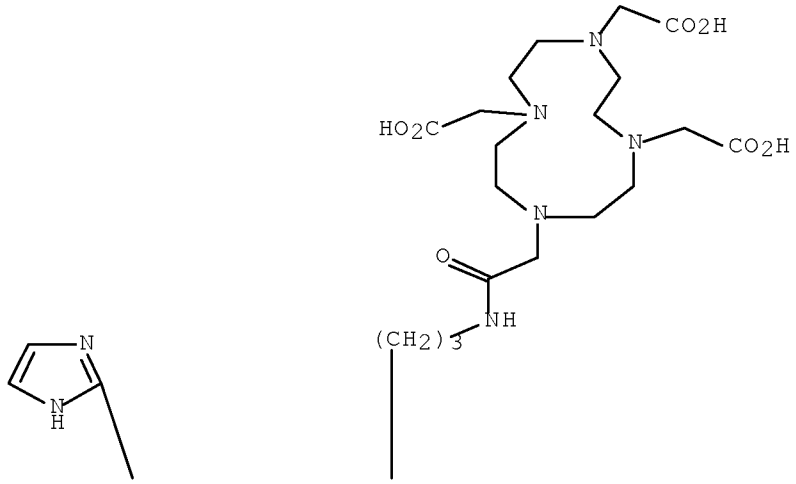
RN 277315-75-0 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-oxoethyl]-, tris(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

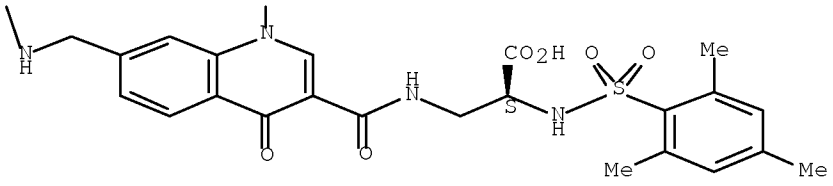
CRN 277315-74-9
CMF C45 H61 N11 O13 S

Absolute stereochemistry.

PAGE 1-A

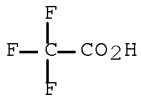


PAGE 2-A



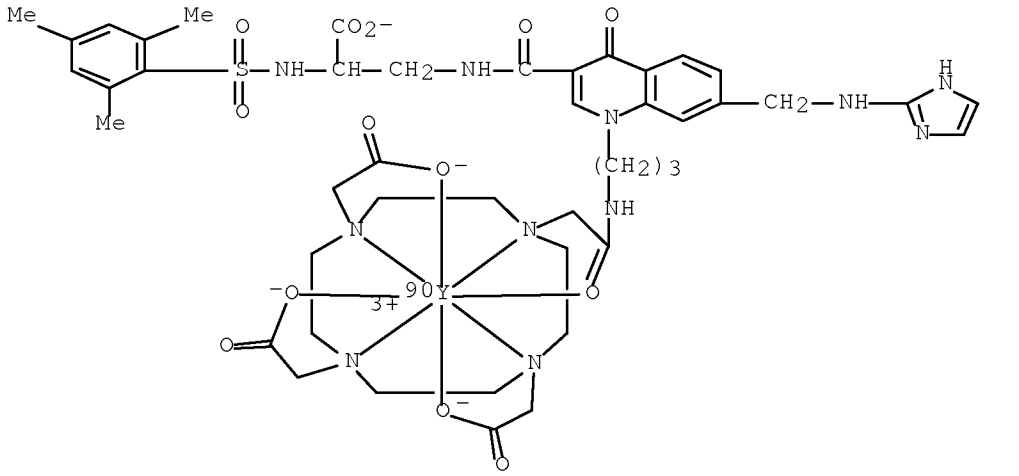
CM 2

CRN 76-05-1
CMF C2 H F3 O2



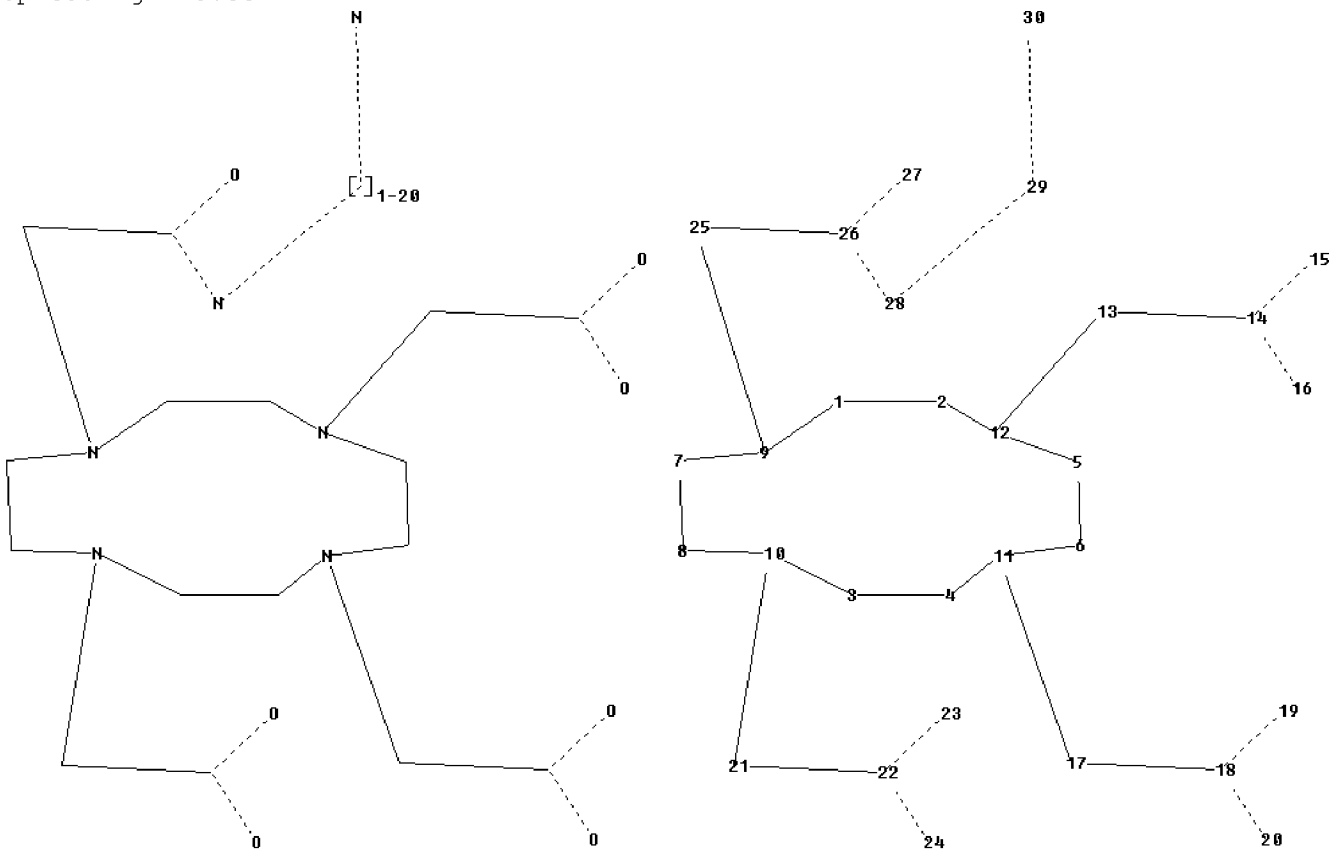
RN 278173-04-9 ZCAPLUS
CN Yttrate(1-)-90Y, [10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(4-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-, hydrogen (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

```
=> file registry
FILE 'REGISTRY' ENTERED AT 10:26:43 ON 21 FEB 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   20 FEB 2008  HIGHEST RN 1004854-20-9
DICTIONARY FILE UPDATES:  20 FEB 2008  HIGHEST RN 1004854-20-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

Uploading L25.str
```

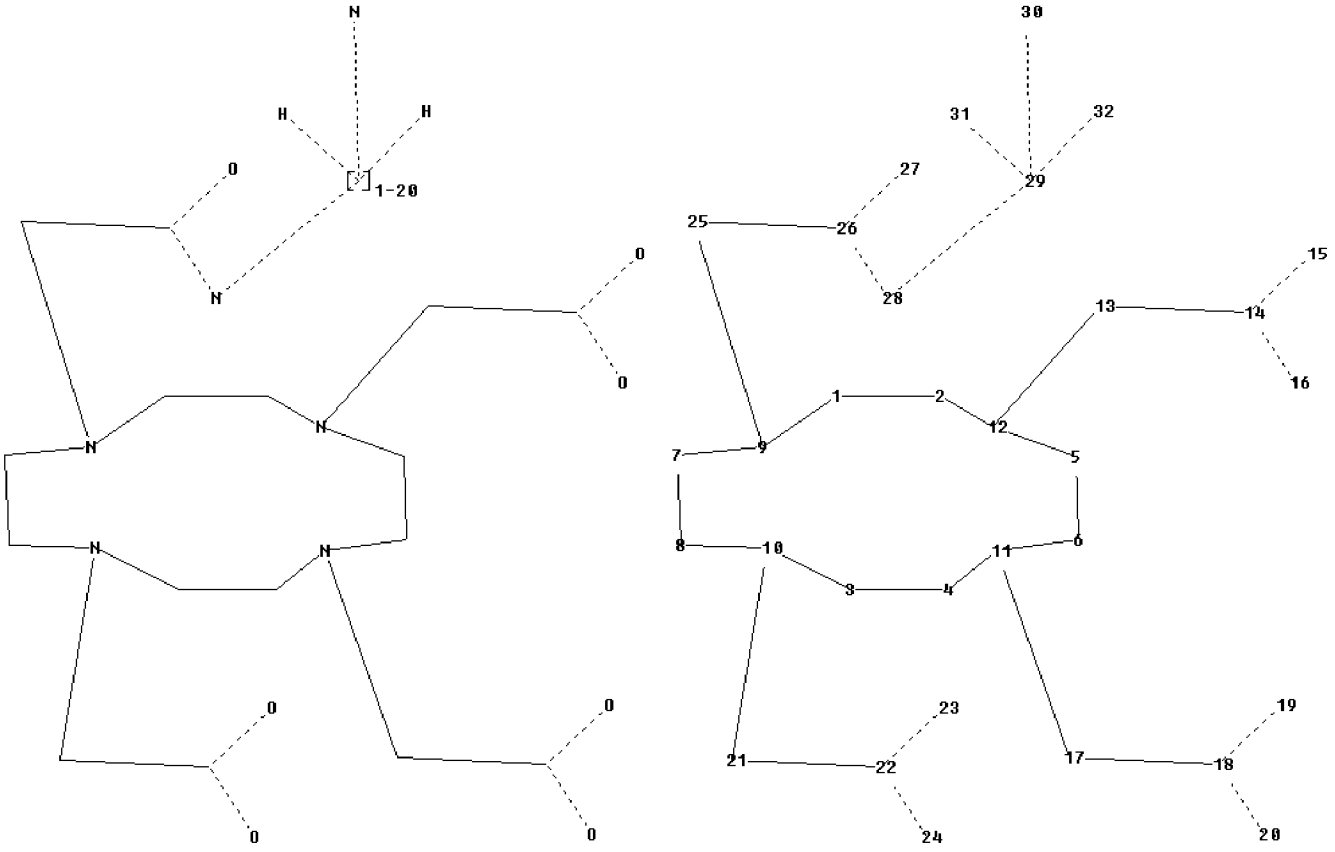



```
ring nodes :
```

1 2 3 4 5 6 7 8 9 10 11 12
ring/chain nodes :
13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
ring/chain bonds :
9-25 10-21 11-17 12-13 13-14 14-16 14-15 17-18 18-20 18-19 21-22 22-24
22-23 25-26 26-28 26-27 28-29 29-30
ring bonds :
1-2 1-9 2-12 3-4 3-10 4-11 5-6 5-12 6-11 7-8 7-9 8-10
exact/norm bonds :
1-2 1-9 2-12 3-4 3-10 4-11 5-6 5-12 6-11 7-8 7-9 8-10 9-25 10-21 11-
17
12-13 13-14 14-16 14-15 17-18 18-20 18-19 21-22 22-24 22-23 25-26 26-28
26-27 28-29
29-30

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS
22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS
30:CLASS

Uploading L47.str



chain nodes :
31 32
ring nodes :

```
1  2  3  4  5  6  7  8  9  10  11  12
ring/chain nodes :
13  14  15  16  17  18  19  20  21  22  23  24  25  26  27  28  29  30
chain bonds :
29-31  29-32
ring/chain bonds :
9-25  10-21  11-17  12-13  13-14  14-16  14-15  17-18  18-20  18-19  21-22  22-24
22-23  25-26  26-28  26-27  28-29  29-30
ring bonds :
1-2  1-9  2-12  3-4  3-10  4-11  5-6  5-12  6-11  7-8  7-9  8-10
exact/norm bonds :
1-2  1-9  2-12  3-4  3-10  4-11  5-6  5-12  6-11  7-8  7-9  8-10  9-25  10-21  11-
17
12-13  13-14  14-16  14-15  17-18  18-20  18-19  21-22  22-24  22-23  25-26  26-28
26-27  28-29
29-30  29-31  29-32


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS
19:CLASS  20:CLASS  21:CLASS
22:CLASS  23:CLASS  24:CLASS  25:CLASS  26:CLASS  27:CLASS  28:CLASS  29:CLASS
30:CLASS
31:CLASS  32:CLASS




=> file zcaplus
FILE 'ZCAPLUS' ENTERED AT 10:26:46 ON 21 FEB 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS is
strictly prohibited.

FILE COVERS 1907 - 21 Feb 2008  VOL 148 ISS 8
FILE LAST UPDATED: 20 Feb 2008  (20080220/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'ZCAPLUS' FILE

=> d stat que L64
L25             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *
```

```
Structure attributes must be viewed using STN Express query preparation.
L29        2020 SEA FILE=REGISTRY SSS FUL L25
L47             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L49         345 SEA FILE=REGISTRY SUB=L29 SSS FUL L47
L50         142 SEA FILE=REGISTRY ABB=ON  PLU=ON  L49 AND M/ELS
L51         203 SEA FILE=REGISTRY ABB=ON  PLU=ON  L49 NOT L50
L56         112 SEA FILE=REGISTRY ABB=ON  PLU=ON  L50 AND LNTH/PG
L62       25232 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  ?SCAFFOLD?/BI
L64           2 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  (L51 OR L56) AND L62


=> d stat que L65
L25             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L29        2020 SEA FILE=REGISTRY SSS FUL L25
L47             STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L49         345 SEA FILE=REGISTRY SUB=L29 SSS FUL L47
L50         142 SEA FILE=REGISTRY ABB=ON  PLU=ON  L49 AND M/ELS
L51         203 SEA FILE=REGISTRY ABB=ON  PLU=ON  L49 NOT L50
L56         112 SEA FILE=REGISTRY ABB=ON  PLU=ON  L50 AND LNTH/PG
L60      641196 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  ?TUMOUR?/BI OR ?TUMOR?/BI
L65          40 SEA FILE=ZCAPLUS ABB=ON  PLU=ON  (L51 OR L56) AND L60


=> s L64-L65 not  L79,L73,L74
L80         32 (L64 OR L65) NOT  (L79 OR L73 OR L74)

=> d ibib abs hitind hitstr L80 1-32

L80  ANSWER 1 OF 32  ZCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2008:39770  ZCAPLUS  Full-text
DOCUMENT NUMBER:          148:145033
TITLE:                    Preparation of gastrin-releasing peptide compounds as
                          diagnostic imaging agents or radiotherapeutic agents
                          and methods of their use for treating prostate cancer
INVENTOR(S):              Cappelletti, Enrico; Lattuada, Luciano; Linder, Karen
                          E.; Marinelli, Edmund; Nanjappan, Palaniappa; Nunn,
                          Adrian D.; Raju, Natarajan; Ramalingam, Kondareddiar;
                          Swenson, Rolf E.; Tweedle, Michael; Maddalena, Mary
                          Ellen
PATENT ASSIGNEE(S):       Bracco Imaging S.p.A., Italy
SOURCE:                   U.S. Pat. Appl. Publ., 218pp., Cont.-in-part of U.S.
                          Ser. No. 352,156.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   6
PATENT INFORMATION:
```

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2008008649	A1	20080110	US 2007-751337	20070521
US 2004136906	A1	20040715	US 2003-341577	20030113
US 7226577	B2	20070605		
WO 2004065407	A2	20040805	WO 2003-US41328	20031224
WO 2004065407	A3	20040923		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004253225	A1	20041216	US 2004-828925	20040420
US 2006018830	A1	20060126	US 2005-165721	20050624
US 2006239914	A1	20061026	US 2006-352156	20060210
IN 2006CN02330	A	20070706	IN 2006-CN2330	20060626

PRIORITY APPLN. INFO.:	US 2003-341577	A2	20030113
	WO 2003-US41328	A2	20031224
	US 2004-828925	A2	20040420
	US 2005-165721	A2	20050624
	US 2006-352156	A2	20060210
	WO 2004-US22115	W	20040712

AB The invention is related to novel gastrin-releasing peptide (GRP) compds. of formula M-N-O-P-G (M is an optical label or a metal chelator complexed with a radionuclide; N, P are null, an amino acid or other linking group; O is an amino acid; at least one of N, O, or P is a non-α-amino acid; G is a GRP receptor targeting peptide) which are useful as diagnostic imaging agents or radiotherapeutic agents. The invention is also related to methods for treating prostate tumors or of delaying the progression of prostate tumors, including, methods of treating bone or soft tissue metastases of prostate cancer, methods for treating hormone sensitive and hormone refractory prostate cancer, methods for delaying the progression of hormone sensitive prostate cancer, for facilitating combination therapy in patients with hormone sensitive prostate cancer and for decreasing aberrant vascular permeability in patients with hormone sensitive prostate cancer. Thus, DOTA-Gly-4-NHC6H4CO-L-Gln-L-Trp-L-Ala-L- Val-Gly-L-His-L-Leu-L-Met-NH2 (DOTA = 1,4,7,10-tetraazacyclododecane- 1,4,7,10-tetraacetic acid residue) was prepared by the solid-phase method and complexed with 177Lu for cell binding, biodistribution and aberrant vascular permeability in LNCaP tumors studies.

INCL 424001690

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 8, 78

IT Antitumor agents
Combination chemotherapy
Human
Radiography
Radiotherapy
(preparation of gastrin-releasing peptide compds. for use as diagnostic imaging agents or radio therapeutic agents)

IT 721936-47-6P 721936-49-8P 721936-51-2P 721936-53-4P 721936-55-6P
721936-57-8P 721936-59-0P 721936-61-4P 721936-63-6P 721936-67-0P
721936-69-2P 721936-71-6P 721936-73-8P 721936-75-0P 721936-76-1P
721936-78-3P 721936-80-7P 721936-82-9P 721936-92-1P 721936-94-3P
721936-96-5P 721936-98-7P 721936-99-8P 721937-01-5P 721937-03-7P
721937-05-9P 721937-07-1P 721937-09-3P 721937-11-7P 721937-13-9P
721937-15-1P 721937-17-3P 721937-19-5P 721937-21-9P 721937-23-1P

721937-25-3P 721937-27-5P 721937-29-7P 721937-31-1P 721937-33-3P
721937-35-5P 721937-37-7P 721937-40-2P 721937-42-4P 721937-48-0P
721937-50-4P 721937-52-6P 721937-54-8P 721937-58-2P 721937-60-6P
721937-62-8P 721937-64-0P 721937-66-2P 721937-68-4P 721937-70-8P
721937-72-0P 721937-74-2P 721937-76-4P 721937-78-6P 721937-80-0P
721937-82-2P 721937-84-4P 721937-86-6P 721937-88-8P
721937-90-2P 721937-92-4P 721937-94-6P 721937-96-8P
721937-98-0P 721938-00-7P 721938-02-9P 721938-04-1P 721938-06-3P
721938-08-5P 721938-10-9P 721938-12-1P 721938-14-3P 721938-16-5P
721938-18-7P 721938-20-1P 721938-22-3P 721938-24-5P 721938-26-7P
721938-28-9P 721938-30-3P 721938-32-5P 721938-34-7P 721938-36-9P
721938-38-1P 721938-39-2P 721938-41-6P 721938-43-8P 721938-45-0P
721938-47-2P 721938-49-4P 721938-51-8P 721938-54-1P 721938-56-3P
721938-58-5P 721938-60-9P 721938-62-1P 721938-64-3P 721938-66-5P
721938-68-7P 721938-70-1P 721938-72-3P 721938-74-5P 721938-76-7P
721938-78-9P 721938-80-3P 721938-83-6P 721938-85-8P 721938-87-0P
721938-89-2P 721938-97-2P 721938-99-4P 721939-01-1P 721939-03-3P
721939-05-5P 721939-06-6P 721939-07-7P 721939-08-8P 721939-10-2P
721939-11-3P 721939-12-4P 721939-14-6P 721939-16-8P 721939-17-9P
721939-18-0P 721939-19-1P 721939-21-5P 721939-23-7P 721939-25-9P
721939-27-1P 721939-29-3P 721939-31-7P 721939-33-9P 721939-35-1P
721939-37-3P 722493-92-7P 722493-93-8P 722493-94-9P 722493-95-0P
722493-96-1P 722493-97-2P 722493-98-3P 722493-99-4P 722494-00-0P
722494-01-1P 722494-02-2P 808112-30-3P 808112-31-4P 808112-32-5P
808112-33-6P 808112-35-8P 808112-37-0P 808112-39-2P
808112-41-6P 808112-43-8P 808112-44-9P 808112-45-0P
808112-46-1P 808112-47-2P 808112-48-3P 808112-49-4P 808112-50-7P
808112-51-8P 808112-52-9P 808112-53-0P 808112-54-1P 808112-55-2P
808112-56-3P 808112-57-4P 808112-58-5P 808112-59-6P 808112-60-9P
808112-61-0P 808112-62-1P 808112-63-2P 808112-64-3P 808112-65-4P
808112-67-6P 808112-68-7P 808112-69-8P 808112-70-1P 808112-71-2P
808112-72-3P 808112-73-4P 808112-74-5P 808112-75-6P
808112-76-7P 808113-15-7P 808113-16-8P 808113-17-9P 808113-18-0P
808113-19-1P 808113-20-4P 808113-21-5P 808113-23-7P 808113-24-8P
808113-25-9P 808113-26-0P 808113-27-1P 808113-28-2P 808113-29-3P
809233-13-4P 809233-16-7P 874367-58-5P 874534-72-2P 874534-73-3P
874537-63-0P 913581-98-3P 913582-14-6P 913582-23-7P 913655-42-2P
913705-76-7P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of gastrin-releasing peptide compds. for use as diagnostic imaging agents or radio therapeutic agents)

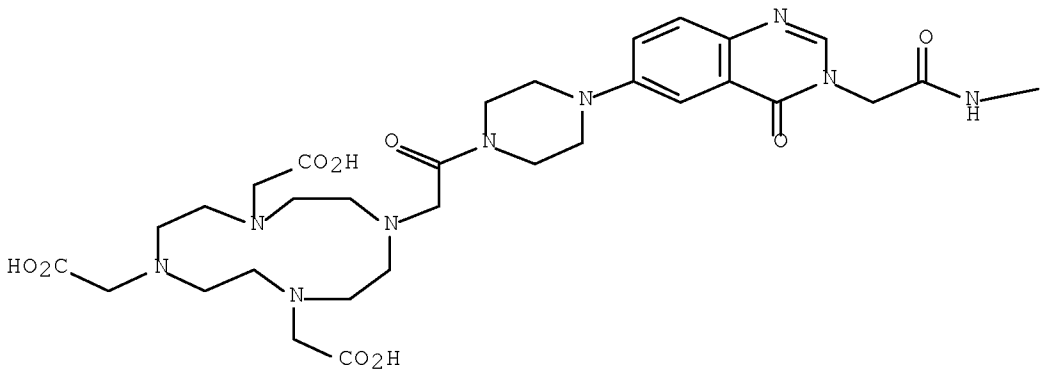
IT 721937-82-2P 721937-90-2P 721937-92-4P
808112-41-6P 808112-74-5P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of gastrin-releasing peptide compds. for use as diagnostic imaging agents or radio therapeutic agents)

RN 721937-82-2 ZCAPLUS

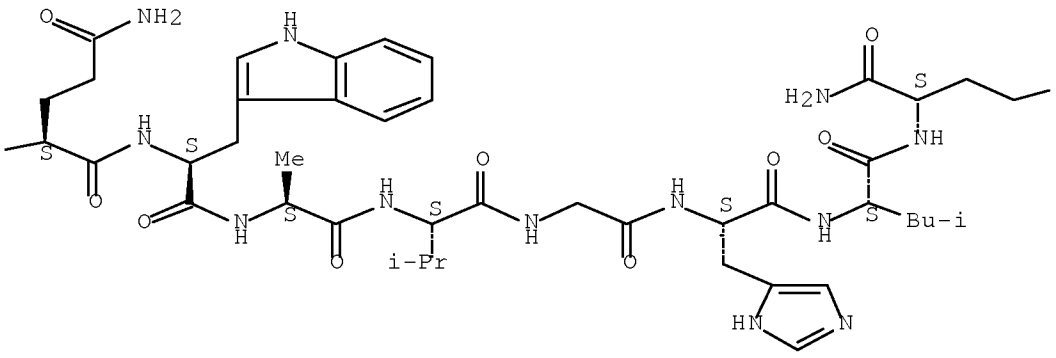
CN L-Methioninamide, N2-[[4-oxo-6-[4-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-1-piperazinyl]-3(4H)-quinazolinyl]acetyl]-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



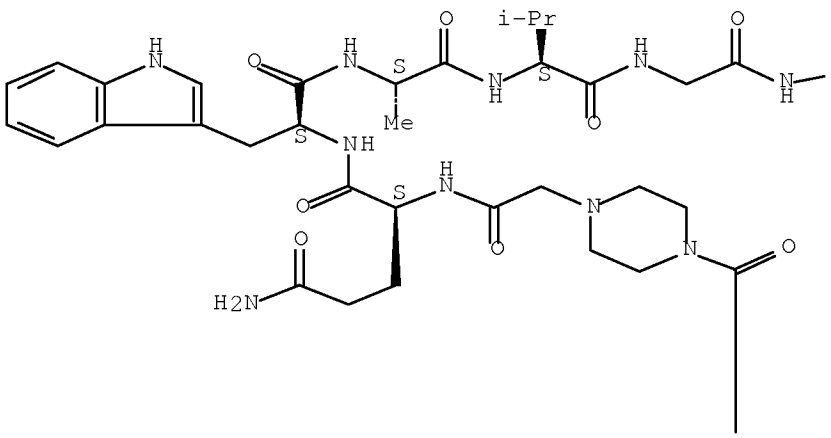
PAGE 1-C

RN 721937-90-2 ZCAPLUS

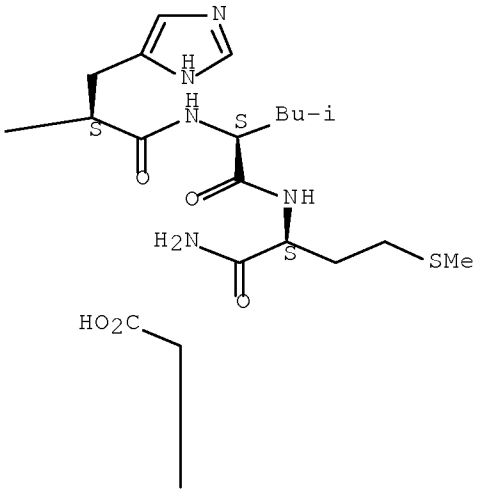
CN L-Methioninamide, N2-[[4-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-1-piperazinyl]acetyl]-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

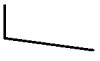
PAGE 1-A



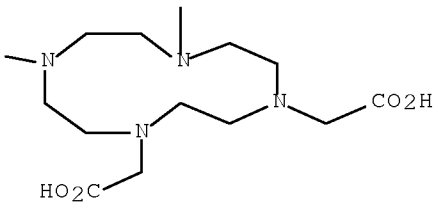
PAGE 1-B



PAGE 2-A



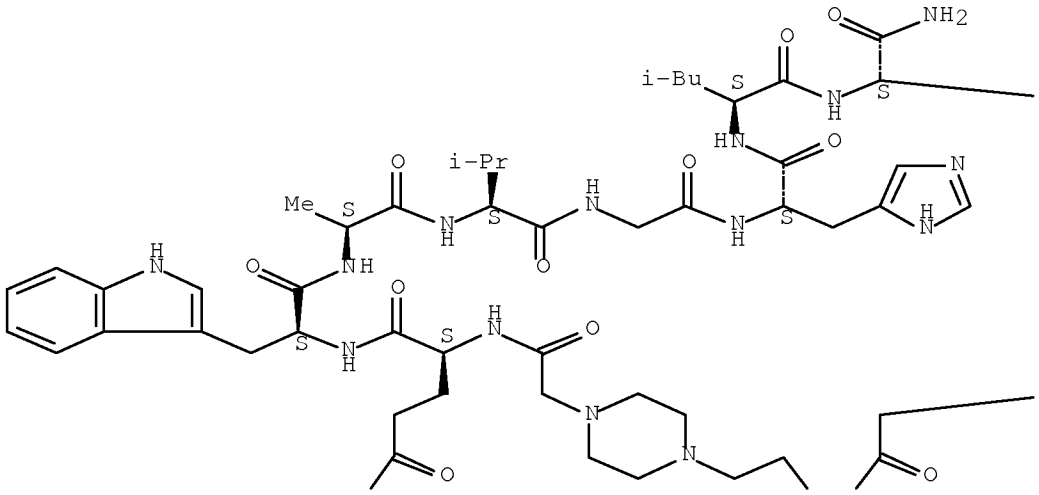
PAGE 2-B



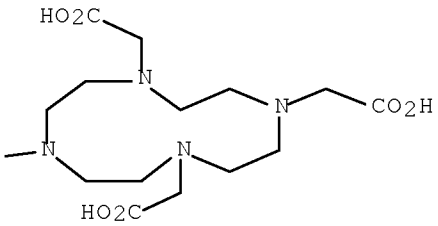
RN 721937-92-4 ZCAPLUS
CN L-Methioninamide, N2-[[4-[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]-1-piperazinyl]acetyl]-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

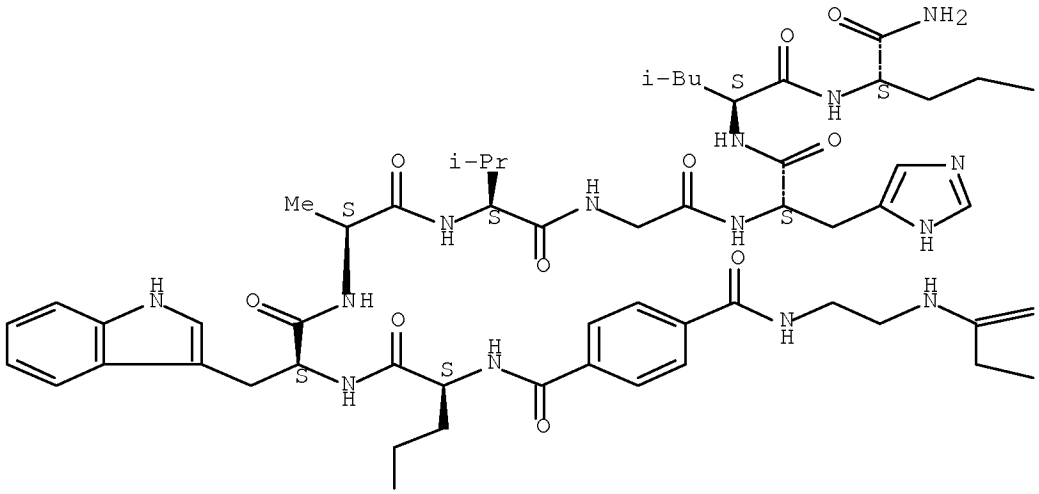


PAGE 2-A

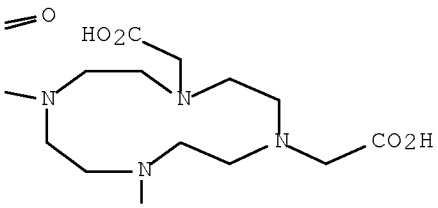
RN 808112-41-6 ZCAPLUS
CN L-Methioninamide, N2-[4-[[[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]carbonyl]benzoyl]-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

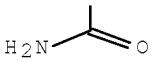
PAGE 1-A



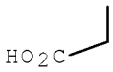
PAGE 1-B



PAGE 2-A



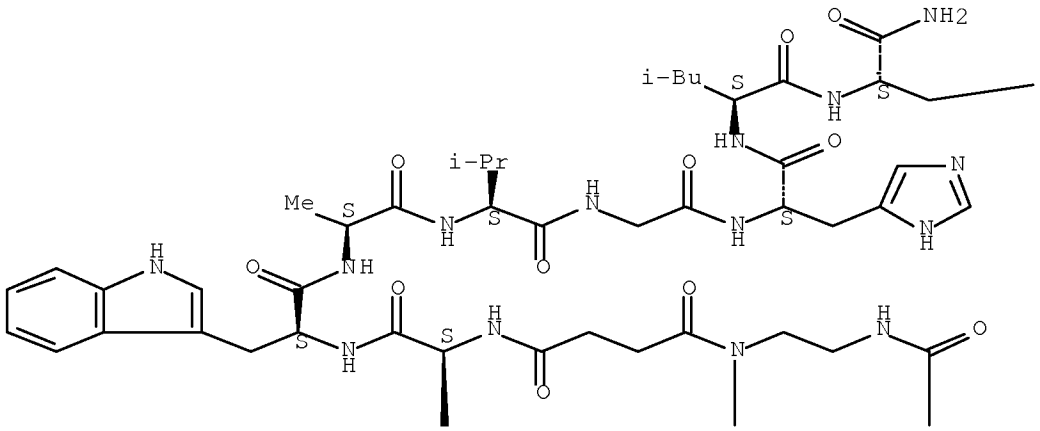
PAGE 2-B



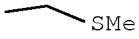
RN 808112-74-5 ZCAPLUS
CN L-Methioninamide, N2-[4-[bis[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]-1,4-dioxobutyl]-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

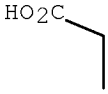
Absolute stereochemistry.

PAGE 1-A

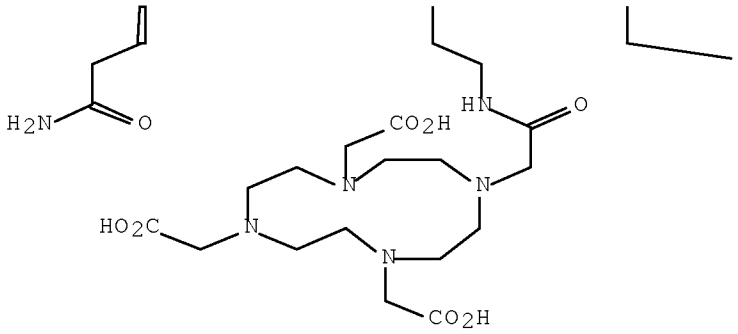


PAGE 1-B

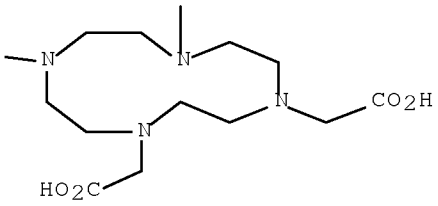




PAGE 2-A



PAGE 2-B



L80 ANSWER 2 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1006173 ZCAPLUS Full-text
DOCUMENT NUMBER: 148:3337
TITLE: In vivo evaluation of a PAMAM-cystamine-(Gd-DO3A) conjugate as a biodegradable macromolecular MRI contrast agent
AUTHOR(S): Xu, Rongzuo; Wang, Yanli; Wang, Xuli; Jeong, Eun-Kee; Parker, Dennis L.; Lu, Zheng-Rong
CORPORATE SOURCE: Dep. Parmaceutics and Pharmaceutical Chem., Univ. Utah, Salt Lake City, UT, 84108, USA
SOURCE: Experimental Biology and Medicine (Maywood, NJ, United States) (2007), 232(8), 1081-1089
CODEN: EBMMBE; ISSN: 1535-3702
PUBLISHER: Society for Experimental Biology and Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Macromol. Gd(III) chelates are superior magnetic resonance imaging (MRI) contrast agents for blood pool and tumor imaging. However, their clin. development is limited by the safety concerns related to the slow excretion and long-term gadolinium tissue accumulation. A generation 6 PAMAM Gd(III) chelate conjugate with a cleavable disulfide spacer, PAMAM-G6-cystamine-(Gd-DO3A)1 was prepared as a biodegradable macromol. MRI contrast agent with rapid excretion from the body. T1 and T2 relaxivities of the contrast agent were 11.6 and 13.3 mM-1 sec-1 at 3T, resp. Blood pool and tumor contrast enhancement of the agent were evaluated in female nude mice bearing MDA-MB-231 human breast carcinoma xenograft swith a nondegradable conjugate PAMAM-G6-(Gd-DO3A) as a control. PAMAM-G6-cystamine-(Gd-DO3A) resulted in significant contrast enhancement in the blood for about 5 mins, and Gd-DO3A was released

from the conjugate and rapidly excreted via renal filtration after the disulfide spacer was cleaved. The nondegradable control had much longer blood circulation and excreted more slowly from the body. PAMAM-G6-cystamine-(Gd-DO3A) also resulted in more prominent tumor contrast enhancement than the control. However, PAMAM-G6-cystamine-(Gd-DO3A) demonstrated high toxicity due to the intrinsic toxicity of PAMAM dendrimers. In conclusion, although PAMAM-G6-cystamine-(Gd-DO3A) showed some advantages compared with the nondegradable control. PAMAM dendrimers are not suitable carriers for biodegradable macromol. MRI contrast agents, due to their high toxicity.

CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 9, 14

ST MRI contrast PAMAM cystamine GdDO3A conjugate pharmacokinetics tumor imaging; mouse blood clearance MRI contrast agent disulfide spacer toxicity

IT Imaging
(NMR, tumor imaging using; in vivo evaluation of a PAMAM-cystamine-(Gd-DO3A) conjugate as a biodegradable macromol. MRI contrast agent)

IT 958259-88-6P
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(in vivo evaluation of a PAMAM-cystamine-(Gd-DO3A) conjugate as a biodegradable macromol. MRI contrast agent)

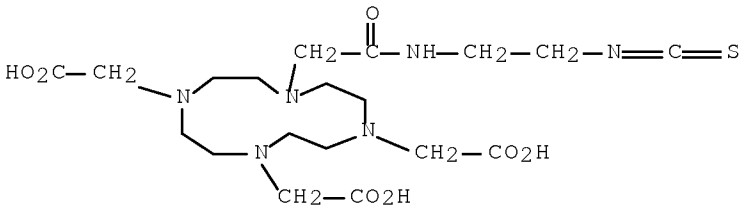
IT 99616-36-1P 150467-20-2P 958259-91-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in vivo evaluation of a PAMAM-cystamine-(Gd-DO3A) conjugate as a biodegradable macromol. MRI contrast agent)

IT 585531-76-6DP, PAMAM dendrimeric gadolinium complexes
958259-88-6DP, PAMAM dendrimeric gadolinium complexes
RL: SPN (Synthetic preparation); PREP (Preparation)
(in vivo evaluation of a PAMAM-cystamine-(Gd-DO3A) conjugate as a biodegradable macromol. MRI contrast agent)

IT 958259-88-6P
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(in vivo evaluation of a PAMAM-cystamine-(Gd-DO3A) conjugate as a biodegradable macromol. MRI contrast agent)

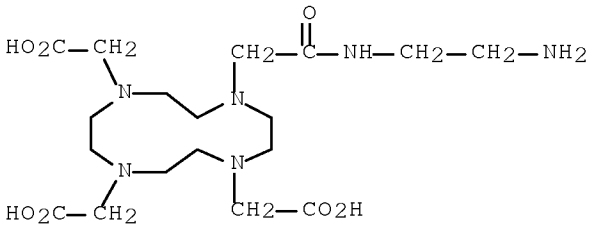
RN 958259-88-6 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-isothiocyanatoethyl)amino]-2-oxoethyl]- (CA INDEX NAME)

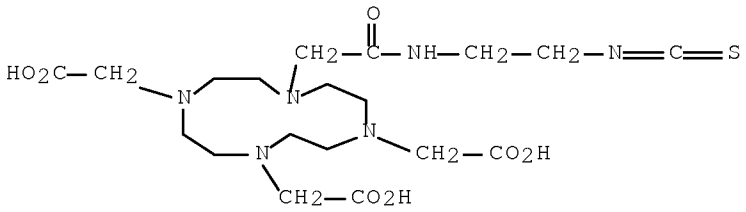


IT 150467-20-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in vivo evaluation of a PAMAM-cystamine-(Gd-DO3A) conjugate as a biodegradable macromol. MRI contrast agent)

RN 150467-20-2 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]- (CA INDEX NAME)



IT 958259-88-6DP, PAMAM dendrimeric gadolinium complexes
RL: SPN (Synthetic preparation); PREP (Preparation)
(in vivo evaluation of a PAMAM-cystamine-(Gd-DO3A) conjugate as a biodegradable macromol. MRI contrast agent)
RN 958259-88-6 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-isothiocyanatoethyl)amino]-2-oxoethyl]- (CA INDEX NAME)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 3 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:969732 ZCAPLUS Full-text
DOCUMENT NUMBER: 147:294732
TITLE: Polyamine-substituted ligands for use as contrast agents
INVENTOR(S): Wolf, Markus; Bauder-Wust, Ulrike; Haberkorn, Uwe; Eisenhut, Michael; Mier, Walter
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 20pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2007202047	A1	20070830	US 2007-649503		20070104
PRIORITY APPLN. INFO.:			US 2006-756352P	P	20060105

OTHER SOURCE(S): MARPAT 147:294732

AB The present invention relates to a polyamine-substituted ligand for the preparation of a contrast agent derived from a chelating mol. selected from the group consisting of 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) and diethylentriamine-pentaacetic acid (DTPA), wherein at least one of the carboxylic groups of the chelating mol. is reacted with an amine of formula HNR1R2 to form an amide bond, wherein R1, R2 are independently selected from the group consisting of H; (CH2)n-NR3R4; and R5; R3, R4 are independently selected from the group consisting of H; (CH2)m-NR6R7; and (CH2)m-1-CH3; R6, R7 are independently selected from the group consisting of H; and (CH2)o-1-CH3; n, m, o are independently 2, 3, or 4; R5 is of formula and optionally at least one of the carboxylic groups of the chelating mol. is further reacted with a monoalkylamine having 1 to 18 carbon atoms to form an amide bond; provided that at least one of R1, R2 is other than H. Furthermore, the invention relates to contrast agents for magnetic resonance imaging (MRI) comprising said ligands and in-vivo diagnostic methods based on MRI using said contrast agents.

INCL 424009363; 534015000; 540474000

CC 8-9 (Radiation Biochemistry)

ST polyamine substituted ligand gadolinium MRI tumor imaging

IT Imaging
(tumor; polyamine-substituted ligands for use as MRI contrast agents)

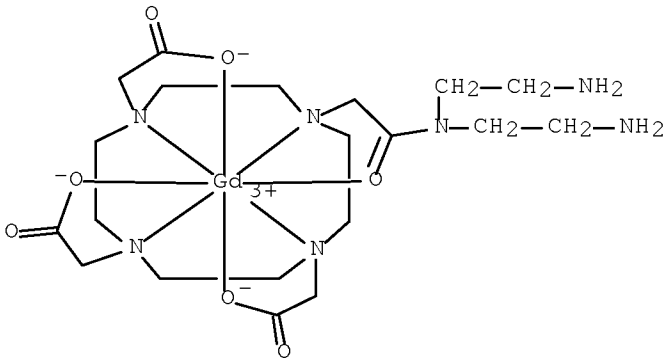
IT 7440-54-2DP, Gadolinium, polyamine-substituted ligand conjugates
947391-67-5P 947391-68-6P 947391-69-7P 947391-70-0P
947391-71-1P 947391-72-2P 947391-73-3P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polyamine-substituted ligands for use as MRI contrast agents)

IT 85503-20-4P 120131-72-8P 134935-60-7P 923952-46-9P 923952-47-0P
923952-48-1P 923952-49-2P 923952-50-5P 947337-79-3P 947337-80-6P
947337-81-7P 947337-82-8P 947337-83-9P
947337-84-0P 947337-85-1P 947337-86-2P 947337-87-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(polyamine-substituted ligands for use as MRI contrast agents)

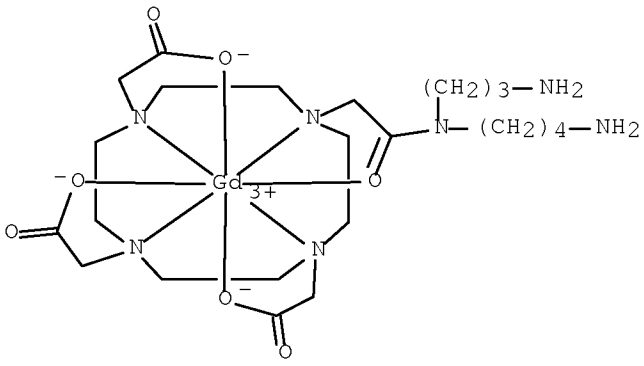
IT 947391-70-0P 947391-71-1P 947391-72-2P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polyamine-substituted ligands for use as MRI contrast agents)

RN 947391-70-0 ZCAPLUS

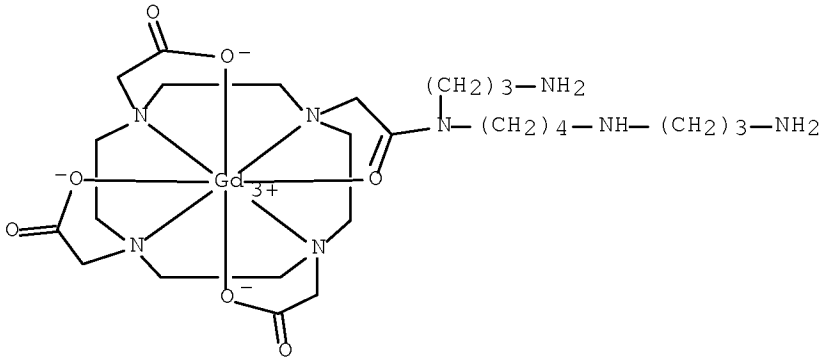
CN Gadolinium, [10-[2-[bis(2-aminoethyl)amino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(8-)-κN7,κN10,κO1,κO4]- (CA INDEX NAME)



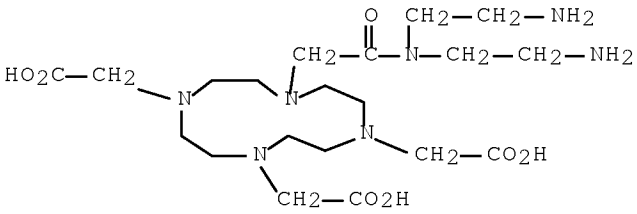
RN 947391-71-1 ZCAPLUS
CN Gadolinium, [10-[2-[(4-aminobutyl)(3-aminopropyl)amino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-
(CA INDEX NAME)



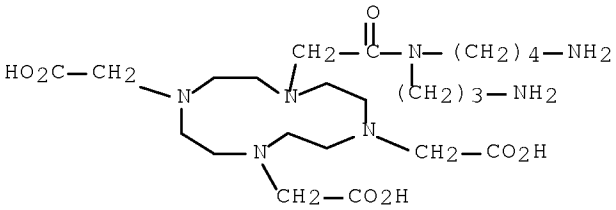
RN 947391-72-2 ZCAPLUS
CN Gadolinium, [10-[2-[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-
(CA INDEX NAME)



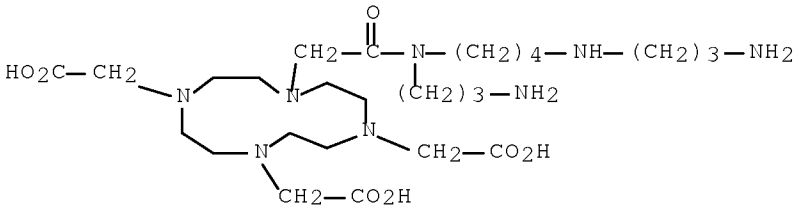
IT 947337-81-7P 947337-82-8P 947337-83-9P
947337-86-2P 947337-87-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(polyamine-substituted ligands for use as MRI contrast agents)
RN 947337-81-7 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[bis(2-aminoethyl)amino]-2-oxoethyl]- (CA INDEX NAME)



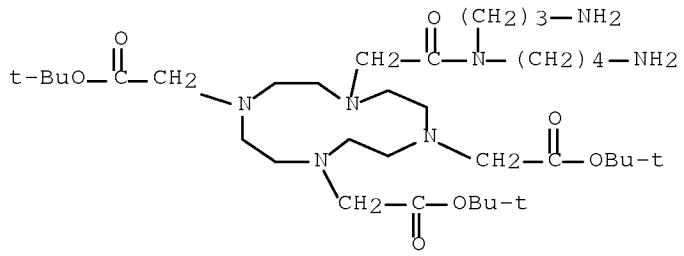
RN 947337-82-8 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(4-aminobutyl)(3-aminopropyl)amino]-2-oxoethyl]- (CA INDEX NAME)



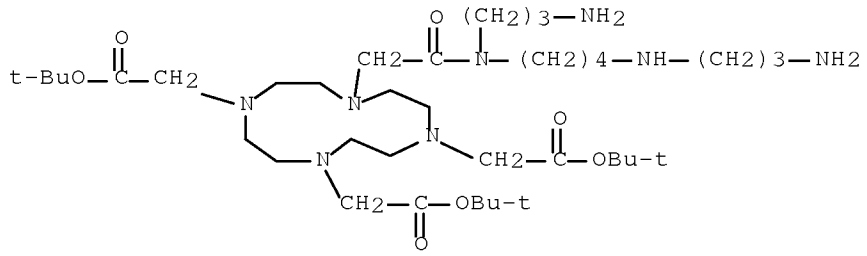
RN 947337-83-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]-2-oxoethyl]- (CA INDEX NAME)



RN 947337-86-2 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(4-aminobutyl)(3-aminopropyl)amino]-2-oxoethyl]-, 1,4,7-tris(1,1-dimethylethyl) ester (CA INDEX NAME)



RN 947337-87-3 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(3-aminopropyl)[4-[(3-aminopropyl)amino]butyl]amino]-2-oxoethyl]-, 1,4,7-tris(1,1-dimethylethyl) ester (CA INDEX NAME)



L80 ANSWER 4 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:960536 ZCAPLUS Full-text
DOCUMENT NUMBER: 147:464287
TITLE: Polymer-based elemental tags for sensitive bioassays
AUTHOR(S): Lou, Xudong; Zhang, Guohua; Herrera, Isaac; Kinach, Robert; Olga, Ornatsky; Baranov, Vladimir; Nitz, Mark; Winnik, Mitchell A.
CORPORATE SOURCE: Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, ON, M5S 3G9, Can.
SOURCE: Angewandte Chemie, International Edition (2007), 46(32), 6111-6114, S6111/1-S6111/5
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A water-soluble polymer bearing multiple metal-chelating ligands has been used as a tag for bioassays with inductively coupled plasma mass spectrometry. The tag was covalently conjugated to antibodies, and the polymer-antibody constructs were loaded with lanthanide ions (Ln3+) and used for the simultaneous assay of five orthogonally labeled antibodies against cell surface antigens that differ in abundance by more than two orders of magnitude.

CC 9-5 (Biochemical Methods)
Section cross-reference(s): 14, 15, 35

IT Acute monocytic leukemia
Acute myeloid leukemia
Chelating agents
Chelation

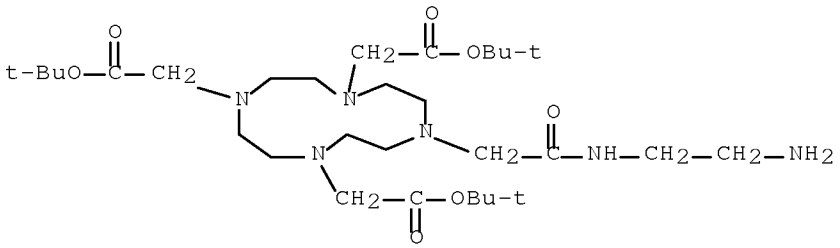
Diagnostic agents
Human
Immunoassay
Molecular recognition
Protein-protein interaction
Tumor markers
(water-soluble polymer bearing multiple metal-chelating ligands tag for bioassays with inductively coupled plasma mass spectrometry applied to leukemia)

IT 115597-84-7 150463-52-8D, t-Bu, dithiobenzoate terminated
173308-19-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(water-soluble polymer bearing multiple metal-chelating ligands tag for bioassays with inductively coupled plasma mass spectrometry applied to leukemia)

IT 100-46-9DP, Benzenemethanamine, reaction with acrylamide/acrylic acid polymer, preparation 150467-20-2DP, reaction with acrylamide/acrylic acid polymer 173308-19-5DP, reaction with acrylamide/acrylic acid polymer
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(water-soluble polymer bearing multiple metal-chelating ligands tag for bioassays with inductively coupled plasma mass spectrometry applied to leukemia)

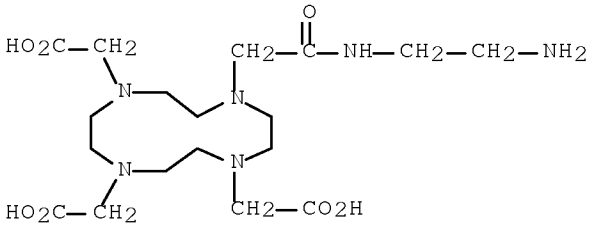
IT 173308-19-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(water-soluble polymer bearing multiple metal-chelating ligands tag for bioassays with inductively coupled plasma mass spectrometry applied to leukemia)

RN 173308-19-5 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-, 1,4,7-tris(1,1-dimethylethyl) ester (CA INDEX NAME)

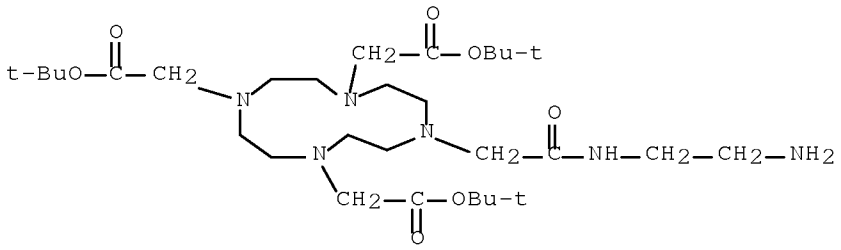


IT 150467-20-2DP, reaction with acrylamide/acrylic acid polymer
173308-19-5DP, reaction with acrylamide/acrylic acid polymer
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(water-soluble polymer bearing multiple metal-chelating ligands tag for bioassays with inductively coupled plasma mass spectrometry applied to leukemia)

RN 150467-20-2 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]- (CA INDEX NAME)



RN 173308-19-5 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-, 1,4,7-tris(1,1-dimethylethyl) ester (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 5 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:545418 ZCAPLUS Full-text
DOCUMENT NUMBER: 147:206685
TITLE: Noninvasive Visualization of Pharmacokinetics, Biodistribution and Tumor Targeting of Poly[N-(2-hydroxypropyl)methacrylamide] in Mice Using Contrast Enhanced MRI
AUTHOR(S): Wang, Yanli; Ye, Furong; Jeong, Eun-Kee; Sun, Yongen; Parker, Dennis L.; Lu, Zheng-Rong
CORPORATE SOURCE: Department of Pharmaceutics and Pharmaceutical Chemistry, University of Utah, Salt Lake City, UT, 84108, USA
SOURCE: Pharmaceutical Research (2007), 24(6), 1208-1216
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: To study a non-invasive method of using contrast enhanced magnetic resonance imaging (MRI) to visualize the real-time pharmacokinetics, biodistribution and tumor accumulation of paramagnetically labeled poly[N-(2-hydroxypropyl)methacrylamide] (PHPMA) copolymer conjugates with different mol. wts. and spacers in tumor-bearing mice. Materials and Methods: Paramagnetically labeled HPMA copolymer conjugates were synthesized by free radical copolymn. of HPMA with monomers containing a chelating ligand, followed by complexation with Gd(OAc)3. A stable paramagnetic chelate, Gd-DO3A, was conjugated to the copolymers via a degradable spacer GlyPheLeuGly

and a non-degradable spacer GlyGly, resp. The conjugates with mol. wts. of 28, 60 and 121 kDa and narrow mol. weight distributions were prepared by fractionation with size exclusion chromatog. The conjugates were injected into athymic nude mice bearing MDA-MB-231 human breast carcinoma xenografts via a tail vein. MR images were acquired before and at various time points after the injection with a 3D FLASH sequence and a 2D spin-echo sequence at 3T. Pharmacokinetics, biodistribution and tumor accumulation of the conjugates were visualized based on the contrast enhancement in the blood, major organs and tumor tissue at various time points. The size effect of the conjugates was analyzed among the conjugates. Results: Contrast enhanced MRI resulted in a real-time, three-dimensional visualization of blood circulation, pharmacokinetics, biodistribution and tumor accumulation of the conjugates, and the size effect on these pharmaceutical properties. HPMA copolymer conjugates with high mol. weight had a prolonged blood circulation time and high passive tumor targeting efficiency. Non-biodegradable HPMA copolymers with mol. wts. higher than the threshold of renal filtration demonstrated higher efficiency for tumor drug delivery than biodegradable poly(L-glutamic acid). Conclusions: Contrast enhanced MRI is an effective method for non-invasive visualization of in vivo properties of the paramagnetically labeled polymer conjugates in preclin. studies.

CC 8-9 (Radiation Biochemistry)

ST contrast MRI gadolinium hydroxypropyl methacrylamide copolymer pharmacokinetics tumor imaging

IT Human
Pharmacokinetics
(MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)

IT Imaging agents
(NMR contrast; MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)

IT Imaging
(NMR; MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)

IT Mammary gland, neoplasm
(carcinoma; MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)

IT Carcinoma
(mammary; MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)

IT Imaging
(tumor; MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)

IT 944834-63-3P 944834-65-5P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)

IT 21442-01-3, N-(2-Hydroxypropyl)methacrylamide 57950-79-5 100424-71-3 912576-20-6 944731-76-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)

IT 944731-74-2P 944731-75-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)

IT 944834-63-3P 944834-65-5P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)

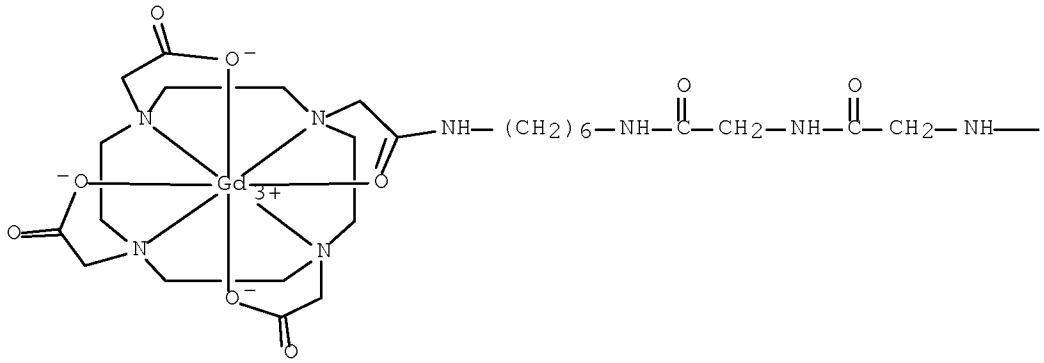
RN 944834-63-3 ZCAPLUS

CN Gadolinium, [N-(2-methyl-1-oxo-2-propen-1-yl)glycyl-N-[6-[[2-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]amino]hexyl]glycinamidato(3-)]-, polymer with N-(2-hydroxypropyl)-2-methyl-2-propenamide (CA INDEX NAME)

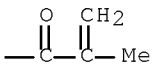
CM 1

CRN 944834-62-2
CMF C30 H49 Gd N8 O10
CCI CCS

PAGE 1-A

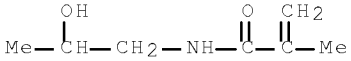


PAGE 1-B



CM 2

CRN 21442-01-3
CMF C7 H13 N O2

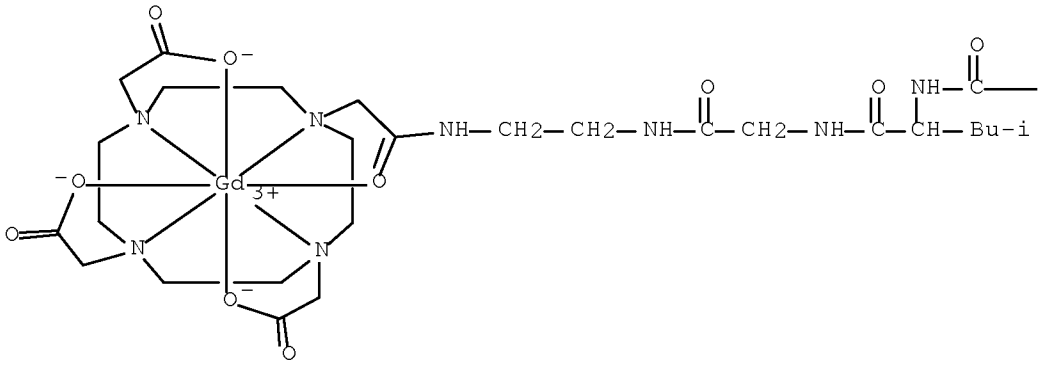


RN 944834-65-5 ZCAPLUS
CN Gadolinium, [N-(2-methyl-1-oxo-2-propen-1-yl)glycyl-L-phenylalanyl-L-leucyl-N-[2-[[2-[4,7,10-tris[(carboxy-κO)methyl]-1,4,7,10-tetraazacyclododec-1-yl-κN1,κN4,κN7,κN10]acetyl-κO]amino]ethyl]glycinamidato(3-)]-, polymer with N-(2-hydroxypropyl)-2-methyl-2-propenamide (CA INDEX NAME)

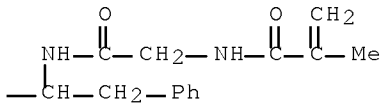
CM 1

CRN 944834-64-4
CMF C41 H61 Gd N10 O12
CCI CCS

PAGE 1-A

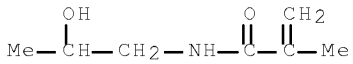


PAGE 1-B



CM 2

CRN 21442-01-3
CMF C7 H13 N O2



IT 912576-20-6 944731-76-4

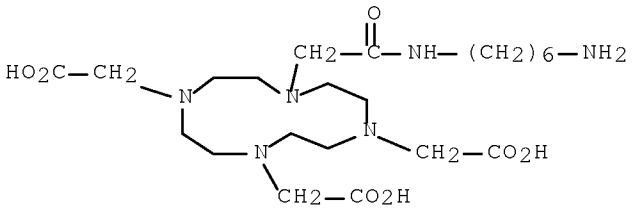
RL: RCT (Reactant); RACT (Reactant or reagent)
(MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)

RN 912576-20-6 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-aminohexyl)amino]-2-oxoethyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

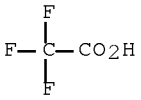
CM 1

CRN 889140-15-2
CMF C22 H42 N6 O7



CM 2

CRN 76-05-1
CMF C2 H F3 O2

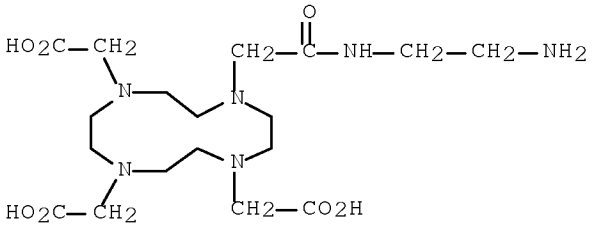


RN 944731-76-4 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

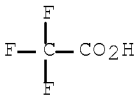
CM 1

CRN 150467-20-2
CMF C18 H34 N6 O7



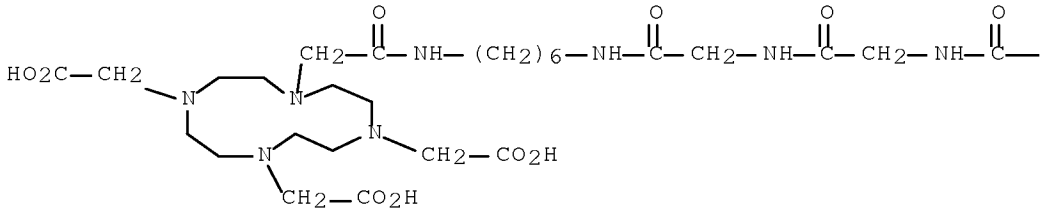
CM 2

CRN 76-05-1
CMF C2 H F3 O2

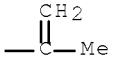


IT 944731-74-2P 944731-75-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(MRI visualization of polyhydroxypropyl methacrylamide pharmacokinetics and tumor targeting)
RN 944731-74-2 ZCAPLUS
CN Glycinamide, N-(2-methyl-1-oxo-2-propen-1-yl)glycyl-N-[6-[[2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]hexyl]- (CA INDEX NAME)

PAGE 1-A



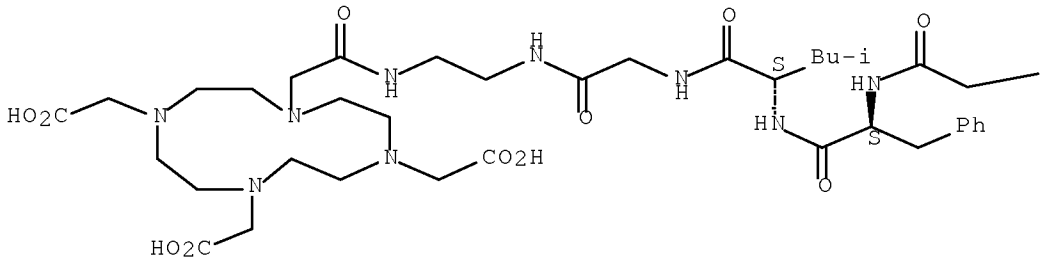
PAGE 1-B



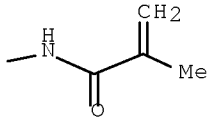
RN 944731-75-3 ZCAPLUS
CN Glycinamide, N-(2-methyl-1-oxo-2-propen-1-yl)glycyl-L-phenylalanyl-L-leucyl-N-[2-[[2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 6 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:402215 ZCAPLUS Full-text
DOCUMENT NUMBER: 146:421772
TITLE: Biotin diamino derivatives and their conjugates with macrocyclic chelating agents
INVENTOR(S): Carminati, Paolo; Ginanneschi, Mauro; Paganelli, Giovanni; Chinol, Marco
PATENT ASSIGNEE(S): Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Italy
SOURCE: PCT Int. Appl., 25pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007039437	A1	20070412	WO 2006-EP66440	20060918

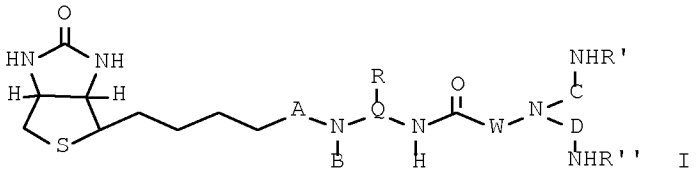
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,

RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

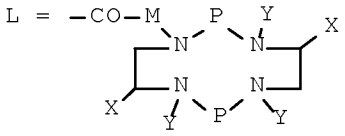
PRIORITY APPLN. INFO.: EP 2005-21034 A 20050927

OTHER SOURCE(S): CASREACT 146:421772; MARPAT 146:421772

GI



I



AB Biotin diamino derivs. I [A = CH2, C:O; B = H, CHO, CO2H; C = (CH2)c; D = (CH2)d; W = C1-12-alkylene, C2-12-alkenylene, functionalized polyethylene glycol, C6-10-aromatic residue, glucofuranosyl residue; R = linear or branched C1-4-alkyl, cycloalkyl, heterocycle, (CH2)qT; T = SMe, OH, CO2H; Q = 0, 1, 2; R', R'' = L; M = (CH2)m; P = (CH2)p; X = H, CH2U, (CHJ)oZ; Y = H, (un)branched C1-44-alkyl, (CH2)mCO2H; U = Me, Et, C6H4NH2-4; Z = NH2, NHC(:NH)NH2, SR2, 5- or 6-membered heterocycle containing one or more O, S, NR1; R1 = H, linear or branched C1-4-alkyl; R2 = linear or branched C1-4-alkyl; J = H, Me, Et; n = 4 - 12; a, b = 0 - n-1; c, d = 3 - 10; m = 1 - 3; o = 1 - 5; p = 2, 3] are described. Processes for their preparation, and their uses for the preparation of conjugates with radionuclides for use in human and animal therapy and diagnostics, particularly for the diagnosis and therapy of pathol. conditions such as tumors. Thus, I [A = W = CH2, B = R = H, Q = (CH2)6, c = d = 3, R' = R'' = 4,7,10-tri(carboxymethyl)- 1,4,7,10-tetrazacyclododecane-1-acetyl] was prepared from reduced biotin N-hexylamide via acylation with N,N-bis[3-[(9- fluorenylmethoxycarbonyl)amino]propyl]glycine potassium sulfate, deprotection with piperidine in DMF and acylation with DOTA.

CC 26-8 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 8, 63, 78

IT Radiopharmaceuticals
(antitumor; preparation of biotin conjugates with macrocyclic amines for therapeutic use as chelating agents)

IT Antitumor agents
Neoplasm
(radiopharmaceuticals; preparation of biotin conjugates with macrocyclic amines for therapeutic use as chelating agents)

IT 934166-99-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(preparation of biotin conjugates with macrocyclic amines for therapeutic use as chelating agents)

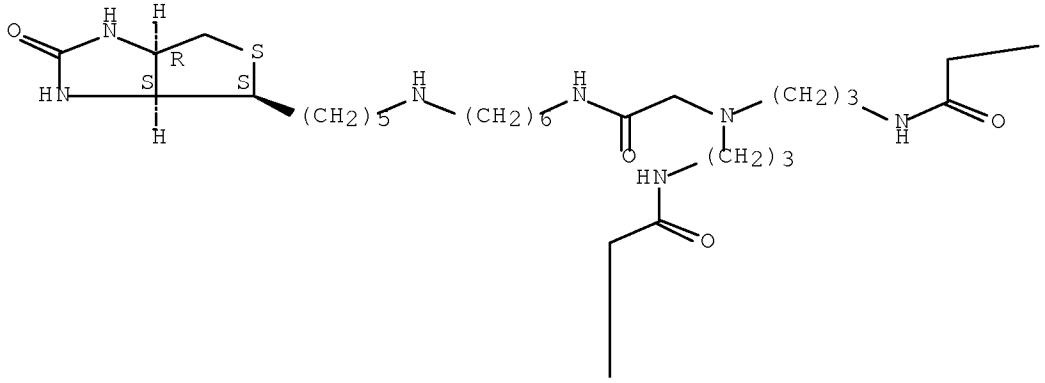
IT 934166-99-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of biotin conjugates with macrocyclic amines for therapeutic use as chelating agents)

RN 934166-99-1 ZCAPLUS

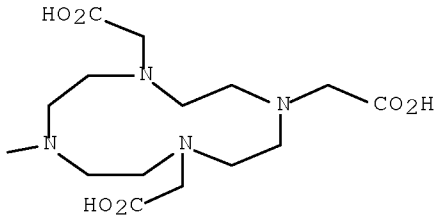
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[[[2-[[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]pentyl]amino]hexyl]amino]-2-oxoethyl]imino]bis[3,1-propanediylimino(2-oxo-2,1-ethanediyl)]]bis- (CA INDEX NAME)

Absolute stereochemistry.

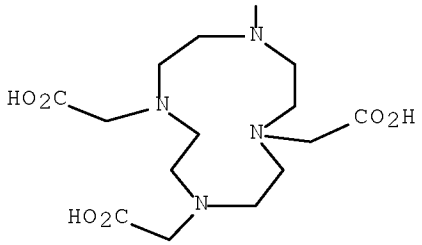
PAGE 1-A



PAGE 1-B



PAGE 2-A



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 7 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:377649 ZCAPLUS Full-text
DOCUMENT NUMBER: 147:66371
TITLE: Physicochemical and MRI characterization of Gd3+-loaded polyamidoamine and hyperbranched dendrimers
AUTHOR(S): Jaszberenyi, Zoltan; Moriggi, Loieck; Schmidt, Philipp; Weidensteiner, Claudia; Kneuer, Rainer; Merbach, Andre E.; Helm, Lothar; Toth, Eva
CORPORATE SOURCE: Institut des Sciences et Ingenierie Chimiques, Ecole Polytechnique Federale de Lausanne, ISIC, BCH, Lausanne, 1015, Switz.
SOURCE: JBIC, Journal of Biological Inorganic Chemistry (2007), 12(3), 406-420
CODEN: JJBCFA; ISSN: 0949-8257
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Generation 4 polyamidoamine (PAMAM) and, for the first time, hyperbranched poly(ethylene imine) or polyglycerol dendrimers have been loaded with Gd3+ chelates, and the macromol. adducts have been studied in vitro and in vivo with regard to MRI contrast agent applications. The Gd3+ chelator was either a tetraazatetracarboxylate DOTA-pBn4- or a tetraazatricarboxylate monoamide DO3A-MA3- unit. The water exchange rate was determined from a 17O NMR and 1H Nuclear Magnetic Relaxation Dispersion study for the corresponding monomer analogs [Gd(DO3A-AEM)(H2O)] and [Gd(DOTA-pBn- NH2)(H2O)]- (k = 3.4 and 6.6 × 106 s-1, resp.), where H3DO3A-AEM is {4-[(2-acetylaminoethylcarbamoyl)methyl]-7,10-bis(carboxymethyl-1,4,7,10- tetraazacyclododec-1-yl)}-acetic acid and H4DOTA-pBn-NH2 is 2-(4-aminobenzyl)-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid. For the macromol. complexes, variable-field proton relaxivities have been measured and analyzed in terms of local and global motional dynamics by using the Lipari-Szabo approach. At frequencies below 100 MHz, the proton relaxivities are twice as high for the dendrimers loaded with the neg. charged Gd(DOTA-pBn)- in comparison with the analogous mol. bearing the neutral Gd(DO3A-MA). We explained this difference by the different rotational dynamics: the much slower motion of Gd(DOTA-pBn)--loaded dendrimers is likely related to the neg. charge of the chelate which creates more rigidity and increases the overall size of the macromol. compared with dendrimers loaded with the neutral Gd(DO3A-MA). Attachment of poly(ethylene glycol) chains to the dendrimers does not influence relaxivity. Both hyperbranched structures were found to be as good scaffolds as regular PAMAM dendrimers in terms of the proton relaxivity of the Gd3+ complexes. The in vivo MRI studies on tumor-bearing mice at 4.7 T proved that all dendrimeric

complexes are suitable for angiog. and for the study of vasculature parameters like blood volume and permeability of tumor vessels.

CC 6-7 (General Biochemistry)
Section cross-reference(s): 1, 63

IT 941280-58-6P
RL: DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nod c,att o d,mov,joi; physicochem. and MRI characterization of Gd3+-loaded polyamidoamine and hyperbranched dendrimers)

IT 9002-98-6DP, reaction products with PAMAM, gadolinium complexes 9004-74-4DP, PAMAM-PEI derivs. 25618-55-7DP, Polyglycerol, amine-functionalized 26937-01-9DP, reaction products with polyethylenimine, gadolinium complexes 120041-09-0DP, PAMAM-PEI gadolinium dendritic derivs. 123317-52-2DP, PAMAM-PEI gadolinium ethoxylated/polyglycerol dendritic derivs. 940961-69-3P
941280-59-7P
RL: DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(physicochem. and MRI characterization of Gd3+-loaded polyamidoamine and hyperbranched dendrimers)

IT 941280-58-6P
RL: DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nod c,att o d,mov,joi; physicochem. and MRI characterization of Gd3+-loaded polyamidoamine and hyperbranched dendrimers)

RN 941280-58-6 ZCAPLUS

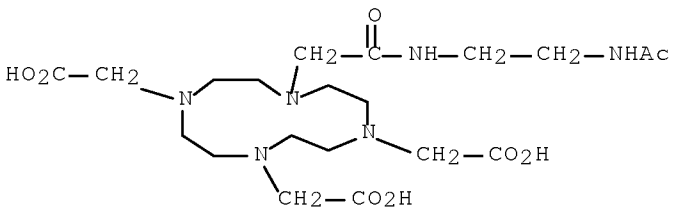
CN Gadolinium, [10-[2-[[2-(acetylamino)ethyl]amino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,κN10,κO1,κO4,κN7]aqua- (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 940961-69-3P
RL: DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(physicochem. and MRI characterization of Gd3+-loaded polyamidoamine and hyperbranched dendrimers)

RN 940961-69-3 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-(acetylamino)ethyl]amino]-2-oxoethyl]- (CA INDEX NAME)



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 8 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:249358 ZCAPLUS Full-text
DOCUMENT NUMBER: 146:501325

TITLE: Synthesis of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers via 1,3-dipolar cycloaddition and their biological evaluation: implications for tumor targeting and tumor imaging purposes

AUTHOR(S): Dijkgraaf, Ingrid; Rijnders, Anneloes Y.; Soede, Annemieke; Dechesne, Annemarie C.; Van Esse, G. Wilma; Brouwer, Arwin J.; Corstens, Frans H. M.; Boerman, Otto C.; Rijkers, Dirk T. S.; Liskamp, Rob M. J.

CORPORATE SOURCE: Department of Medicinal Chemistry and Chemical Biology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, Utrecht, 3508 TB, Neth.

SOURCE: Organic & Biomolecular Chemistry (2007), 5(6), 935-944
CODEN: OBCRAK; ISSN: 1477-0520

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 146:501325

AB The design and synthesis of a series of αVβ3 integrin-directed monomeric, dimeric and tetrameric cyclo[Arg-Gly-Asp-d-Phe-Lys] dendrimers using "click chemical" is described. It was found that the unprotected N-.vepsiln.-azido derivative of cyclo[Arg-Gly-Asp-d-Phe-Lys] underwent a highly chemoselective conjugation to amino acid-based dendrimers bearing terminal alkynes using a microwave-assisted Cu(i)-catalyzed 1,3-dipolar cycloaddn. The αVβ3 binding characteristics of the dendrimers were determined in vitro and their in vivo αVβ3 targeting properties were assessed in nude mice with s.c. growing human SK-RC-52 tumors. The multivalent RGD-dendrimers were found to have enhanced affinity toward the αVβ3 integrin receptor as compared to the monomeric derivative as determined in an in vitro binding assay. In case of the DOTA-conjugated 111In-labeled RGD-dendrimers, it was found that the radiolabeled multimeric dendrimers showed specifically enhanced uptake in αVβ3 integrin expressing tumors in vivo. These studies showed that the tetrameric RGD-dendrimer had better tumor targeting properties than its dimeric and monomeric congeners.

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 28

ST DOTA cyclic RGD peptide conjugated dendrimer prepn tumor imaging; cyclic RGD peptide solid phase prepn DOTA dipolar cycloaddn

IT Cycloaddition reaction
(1,3-dipolar; preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using microwave-assisted dipolar cycloaddn. as the key step for the conjugation)

IT Microwave
(irradiation; preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using microwave-assisted dipolar cycloaddn. as the key step for the conjugation)

IT Antitumor agents
Human
Pharmacokinetics
(preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using microwave-assisted dipolar cycloaddn. as the key step for the conjugation)

IT RGD peptides
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using

microwave-assisted dipolar cycloaddn. as the key step for the conjugation)

IT Imaging
Imaging agents
(tumor; preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using microwave-assisted dipolar cycloaddn. as the key step for the conjugation)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αvβ3; preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using microwave-assisted dipolar cycloaddn. as the key step for the conjugation)

IT 936125-37-0P 936125-39-2P 936235-89-1P
RL: DGN (Diagnostic use); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using microwave-assisted dipolar cycloaddn. as the key step for the conjugation)

IT 99-06-9, 3-Hydroxybenzoic acid, reactions 99-10-5, 3,5-Dihydroxybenzoic acid 106-96-7, Propargyl bromide 107-15-3, 1,2-Ethanediamine, reactions 29022-11-5, Fmoc-Gly-OH 39684-80-5, tert-Butyl (2-bromoethyl)carbamate 71989-14-5 71989-26-9 86123-10-6 137076-54-1 154445-77-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using microwave-assisted dipolar cycloaddn. as the key step for the conjugation)

IT 2150-44-9P, 3,5-Dihydroxybenzoic acid, methyl ester 19438-10-9P, 3-Hydroxybenzoic acid, methyl ester 57260-73-8P 85607-73-4P 160893-68-5P 184916-28-7P 250612-44-3P 664334-21-8P 680572-35-4P 768387-51-5P 866088-22-4P 936125-14-3P 936125-18-7P 936125-20-1P 936125-22-3P 936125-24-5P 936125-26-7P 936125-28-9P 936125-31-4P 942131-93-3P 942131-95-5P 942131-99-9P 942132-29-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using microwave-assisted dipolar cycloaddn. as the key step for the conjugation)

IT 868845-24-3P 868845-25-4P 936125-33-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using microwave-assisted dipolar cycloaddn. as the key step for the conjugation)

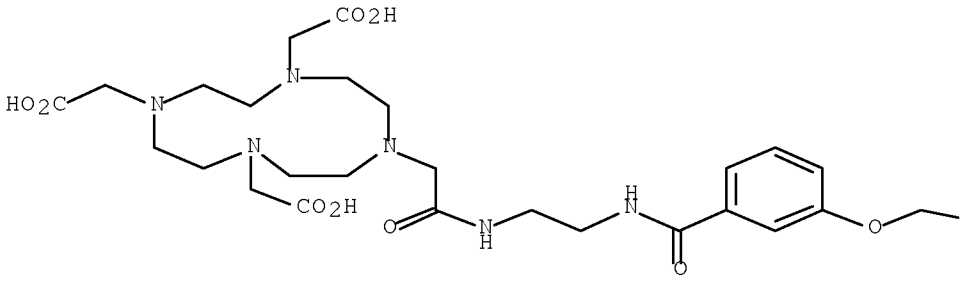
IT 936125-37-0P 936125-39-2P
RL: DGN (Diagnostic use); PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using microwave-assisted dipolar cycloaddn. as the key step for the conjugation)

RN 936125-37-0 ZCAPLUS

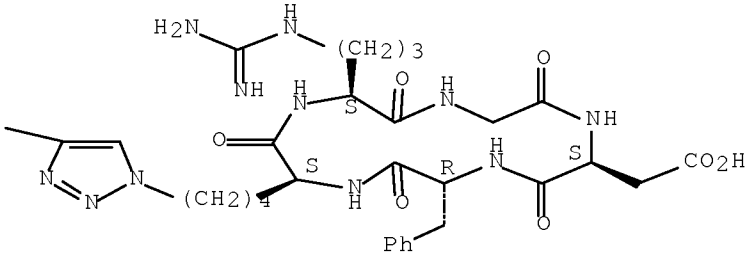
CN Cyclo[L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-6-[4-[[3-[[[2-[[2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]carbonyl]phenoxy]methyl]-1H-1,2,3-triazol-1-yl]-L-norleucyl] (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



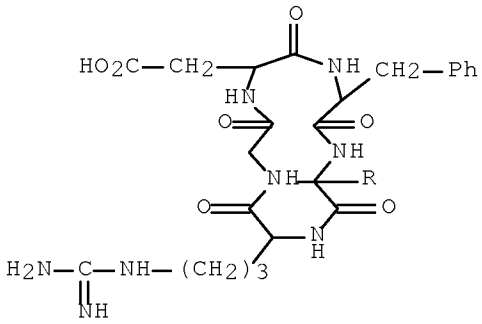
PAGE 1-B

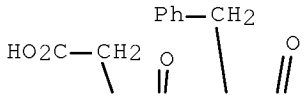


RN 936125-39-2 ZCAPLUS

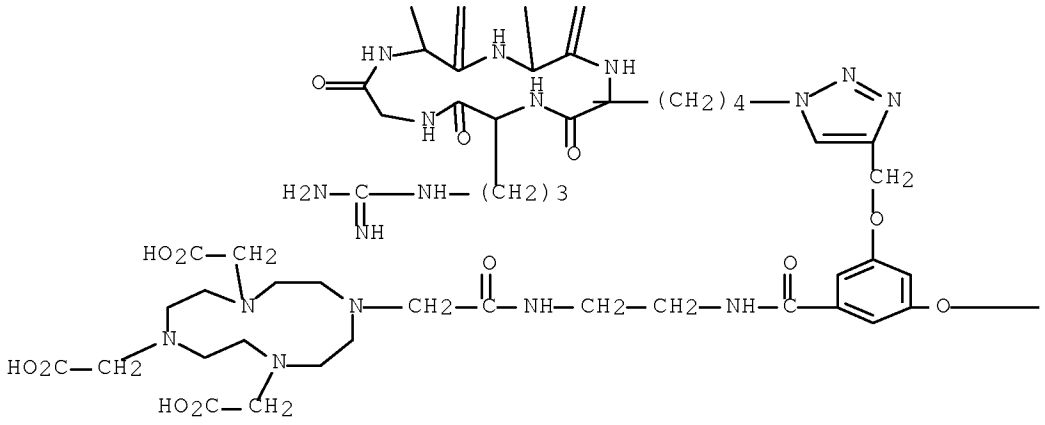
CN Cyclo(L-arginylglycyl-L-α-aspartyl-D-phenylalanyl-L-norleucyl), 56,5'6-[[5-[[[2-[[2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]carbonyl]-1,3-phenylene]bis(oxymethylene-1H-1,2,3-triazole-4,1-diyl)]bis- (CA INDEX NAME)

PAGE 1-A

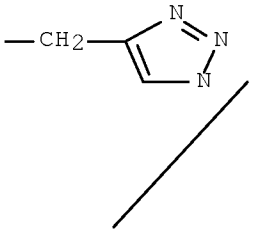




PAGE 2-A



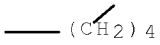
PAGE 2-B



PAGE 3-A

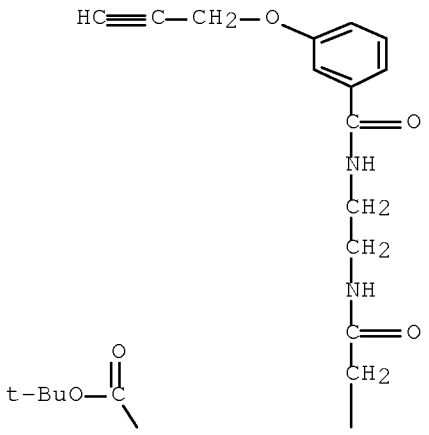
R—

PAGE 3-B

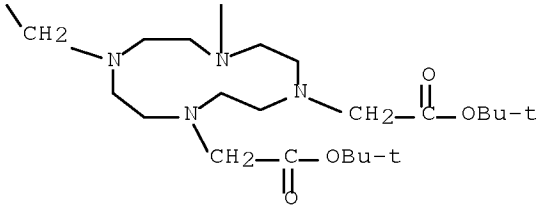


IT 936125-22-3P 936125-24-5P 936125-28-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and tumor targeting and imaging use of DOTA-conjugated multivalent cyclic-RGD peptide dendrimers using microwave-assisted dipolar cycloaddn. as the key step for the conjugation)
RN 936125-22-3 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-oxo-2-[[2-[[3-(2-propyn-1-yloxy)benzoyl]amino]ethyl]amino]ethyl]-, 1,4,7-tris(1,1-dimethylethyl) ester (CA INDEX NAME)

PAGE 1-A

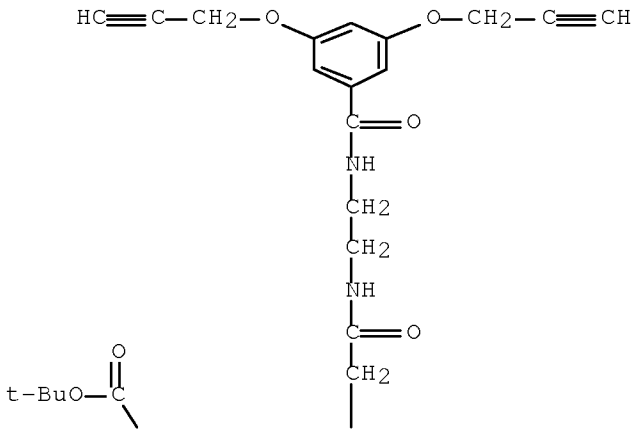


PAGE 2-A

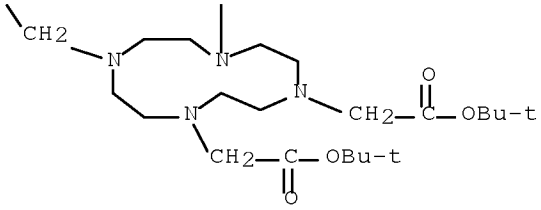


RN 936125-24-5 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[3,5-bis(2-propyn-1-yloxy)benzoyl]amino]ethyl]amino]-2-oxoethyl]-, 1,4,7-tris(1,1-dimethylethyl) ester (CA INDEX NAME)

PAGE 1-A

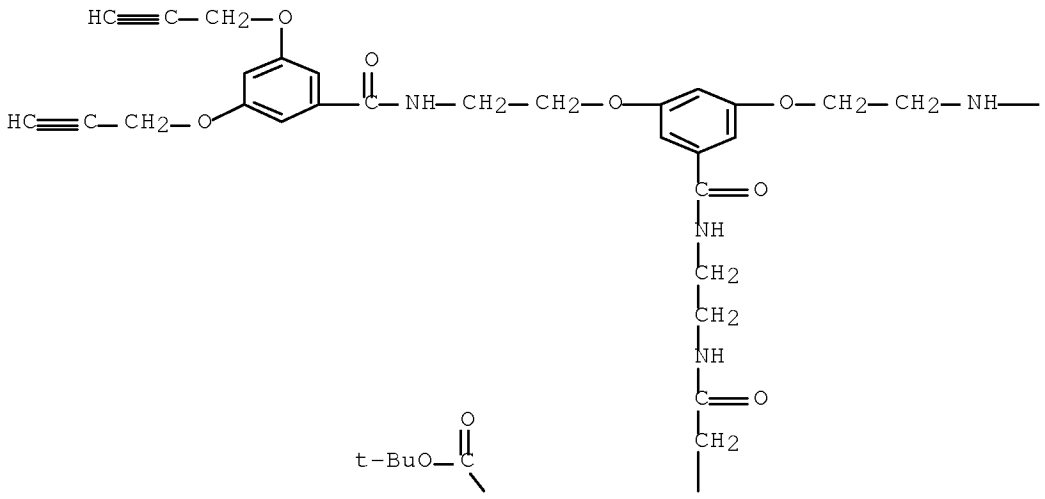


PAGE 2-A

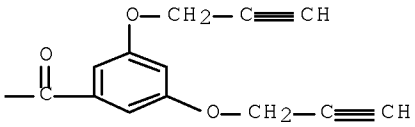


RN 936125-28-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[3,5-bis[2-[[3,5-bis(2-propyn-1-yloxy)benzoyl]amino]ethoxy]benzoyl]amino]ethyl]amino]-2-oxoethyl]-, 1,4,7-tris(1,1-dimethylethyl) ester (CA INDEX NAME)

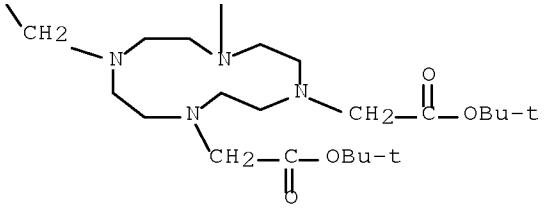
PAGE 1-A



PAGE 1-B



PAGE 2-A



REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 9 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:230231 ZCAPLUS Full-text
DOCUMENT NUMBER: 146:288424
TITLE: Non-invasive diagnostic agents of cancer and methods of diagnosing cancer, especially leukemia and lymphoma
INVENTOR(S): Norenberg, Jeffrey P.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007048216	A1	20070301	US 2006-507846	20060822
PRIORITY APPLN. INFO.:			US 2005-710665P P	20050823

AB The present invention is directed to novel non-invasive diagnostic tools to image cancers, especially, leukemia and non-Hodgkin's lymphomas (NHL) with minimal toxicity in vivo. The present invention represents a clear advance in the art which presently relies on tissue biopsy for diagnoses of these cancers. The novel imaging probe is capable of detecting precancerous cells, as well as their metastatic spread in tissues. This represents a quantum step forward in the diagnosis and staging of NHL using non-invasively mol. imaging techniques. This novel probe will also be useful to monitor patients response to chemotherapy treatments and other interventions or therapies used in the treatment of NHL. Compds. according to the present invention may be used as diagnostic tools for a number of conditions and diseases states as well as therapeutic agents for treating such conditions and disease states.

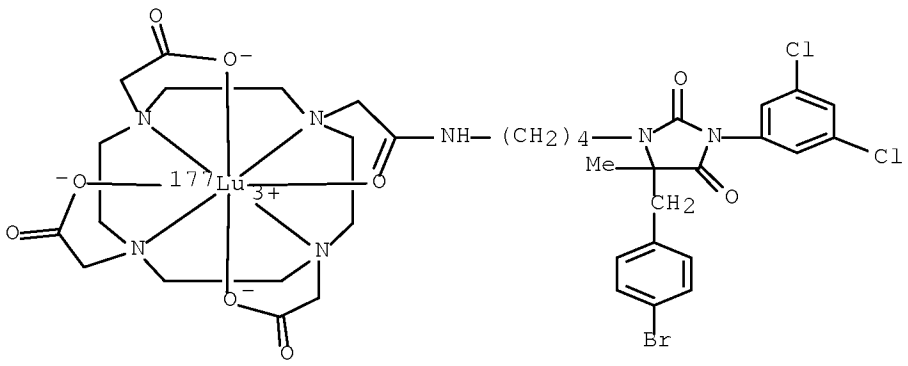
INCL 424001110; 534011000; 534014000
CC 1-6 (Pharmacology)
Section cross-reference(s): 4, 8, 63
IT Acute lymphocytic leukemia
Acute myeloid leukemia
Acute promyelocytic leukemia
Adult T-cell leukemia
Anti-inflammatory agents
Anti-ischemic agents
Antidiabetic agents
Antirheumatic agents
Antitumor agents
Arthritis
Autoimmune disease
Blood analysis
Burn
Cardiopulmonary bypass
Diabetes mellitus
Diagnostic agents
Drug toxicity
Hairy cell leukemia
Hematopoiesis
Human
Imaging
Immunity
Inflammation
Inflammatory bowel diseases
Ischemia
Monocytic leukemia
Multiple sclerosis
Myeloid leukemia
Myocardial infarction
Neoplasm
Osteoarthritis
Polymorphonuclear leukocyte
Psoriasis
Respiratory distress syndrome
Rheumatoid arthritis
Skin, disease

Stem cell
Transplant rejection
Uveitis
Wart
(non-invasive diagnostic agents of cancer and methods of diagnosing cancer, especially leukemia and lymphoma)

IT 927833-57-6 927833-59-8
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)
(non-invasive diagnostic agents of cancer and methods of diagnosing cancer, especially leukemia and lymphoma)

IT 927833-57-6
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DGN (Diagnostic use); PKT (Pharmacokinetics); BIOL (Biological study); USES (Uses)
(non-invasive diagnostic agents of cancer and methods of diagnosing cancer, especially leukemia and lymphoma)

RN 927833-57-6 ZCAPLUS
CN Lutetium-177Lu, [10-[2-[[4-[5-[(4-bromophenyl)methyl]-3-(3,5-dichlorophenyl)-5-methyl-2,4-dioxo-1-imidazolidinyl]butyl]amino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,κN10]- (CA INDEX NAME)



L80 ANSWER 10 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:78033 ZCAPLUS Full-text
DOCUMENT NUMBER: 147:517229
TITLE: PET imaging of apoptosis with 64Cu-labeled streptavidin following pretargeting of phosphatidylserine with biotinylated annexin-V
AUTHOR(S): Cauchon, Nicole; Langlois, Rejean; Rousseau, Jacques A.; Tessier, Guillaume; Cadorette, Jules; Lecomte, Roger; Hunting, Darel J.; Pavan, Roberto A.; Zeisler, Stefan K.; Lier, Johan E.
CORPORATE SOURCE: Sherbrooke Molecular Imaging Centre and Department of Nuclear Medicine and Radiobiology, Faculty of Medicine and Health Sciences, Universite de Sherbrooke, Sherbrooke, QC, Can.
SOURCE: European Journal of Nuclear Medicine and Molecular Imaging (2007), 34(2), 247-258
CODEN: EJNMA6; ISSN: 1619-7070

PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In vivo detection of apoptosis is a diagnostic tool with potential clin. applications in cardiol. and oncol. Radiolabeled annexin-V (anxV) is an ideal probe for in vivo apoptosis detection owing to its strong affinity for phosphatidylserine (PS), the mol. flag on the surface of apoptotic cells. Most clin. studies performed to visualize apoptosis have used 99mTc-anxV; however, its poor distribution profile often compromises image quality. In this study, tumor apoptosis after therapy was visualized by positron emission tomog. (PET) using 64Cu-labeled streptavidin (SAv), following pre-targeting of apoptotic cells with biotinylated anxV. Apoptosis was induced in tumor-bearing mice by photodynamic therapy (PDT) using phthalocyanine dyes as photosensitizers, and red light. After PDT, mice were injected i.v. with biotinylated anxV, followed 2 h later by an avidin chase, and after another 2 h with 64Cu-DOTA-biotin-SAv. PET images were subsequently recorded up to 13 h after PDT. PET images delineated apoptosis in treated tumors as early as 30 min after 64Cu-DOTA-biotin-SAv administration, with tumor-to-background ratios reaching a maximum at 3 h post-injection, i.e., 7 h post-PDT. Omitting the administration of biotinylated anxV or the avidin chase failed to provide a clear PET image, confirming that all three steps are essential for adequate visualization of apoptosis. Furthermore, differences in action mechanisms between photosensitizers that target tumor cells directly or via initial vascular stasis were clearly recognized through differences in tracer uptake patterns detecting early or delayed apoptosis. This study demonstrates the efficacy of a three-step 64Cu pretargeting procedure for PET imaging of apoptosis. These data also confirm the usefulness of small animal PET to evaluate cancer treatment protocols.

CC 8-9 (Radiation Biochemistry)

ST copper 64 DOTA biotin streptavidin PET PDT apoptosis; PET imaging annexin V targeted tumor apoptosis photosensitizer

IT Imaging
(tumor; use of pretargeting procedure of phosphatidylserine with biotinylated annexin-V for PET imaging of apoptosis with 64Cu-SAv complex)

IT 956262-96-7P 956428-39-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(use of pretargeting procedure of phosphatidylserine with biotinylated annexin-V for PET imaging of apoptosis with 64Cu-SAv complex)

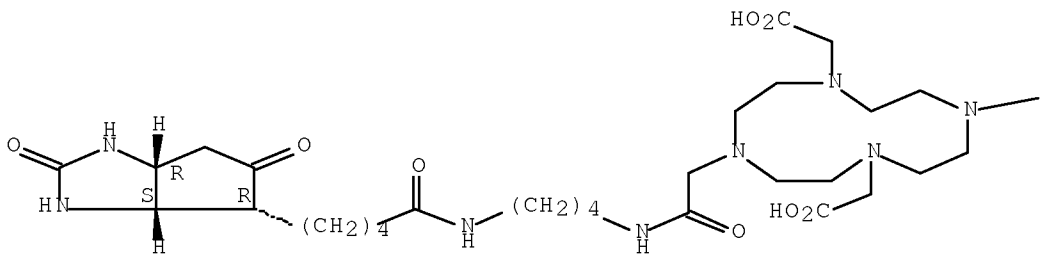
IT 956262-96-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(use of pretargeting procedure of phosphatidylserine with biotinylated annexin-V for PET imaging of apoptosis with 64Cu-SAv complex)

RN 956262-96-7 ZCAPLUS

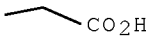
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[4-[[5-[(3aS,4R,6aR)-octahydro-2,5-dioxo-4-cyclopentimidazolyl]-1-oxopentyl]amino]butyl]amino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 11 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:872573 ZCAPLUS Full-text
DOCUMENT NUMBER: 145:425460
TITLE: Noninvasive Visualization of in Vivo Drug Delivery of Poly(L-glutamic acid) Using Contrast-Enhanced MRI
AUTHOR(S): Ye, Furong; Ke, Tianyi; Jeong, Eun-Kee; Wang, Xuli; Sun, Yongen; Johnson, Melody; Lu, Zheng-Rong
CORPORATE SOURCE: Departments of Pharmaceutics and Pharmaceutical Chemistry and Radiology, University of Utah, Salt Lake City, UT, 84108, USA
SOURCE: Molecular Pharmaceutics (2006), 3(5), 507-515
CODEN: MPOHBP; ISSN: 1543-8384
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:425460

AB Biomedical imaging is valuable for noninvasive investigation of in vivo drug delivery with polymer conjugates. It can provide real-time information on pharmacokinetics, biodistribution, and drug delivery efficiency of the conjugates. Noninvasive visualization of in vivo drug delivery of polymer conjugates with contrast-enhanced magnetic resonance imaging (MRI) was studied with paramagnetically labeled poly(L-glutamic acid) in an animal tumor model. Poly(L-glutamic acid) is a biocompatible and biodegradable drug carrier for diagnostics and therapeutics. Poly(L-glutamic acid)-1,6-hexanediamine-(Gd-DO3A) conjugates with mol. wts. of 87, 50, and 28 kDa and narrow mol. weight distributions were prepared and studied in mice bearing MDA-MB-231 human breast cancer xenografts. Contrast-enhanced MRI resulted in real-time and three-dimensional visualization of blood circulation, pharmacokinetics, biodistribution, and tumor accumulation of the conjugates, and the size effect on these pharmaceutics properties. The conjugate of 28 kDa rapidly cleared from the circulation and had a relatively lower tumor accumulation. The conjugates with higher mol. wts. exhibited a more prolonged blood circulation and higher tumor accumulation. The difference between the conjugates of 87

and 50 kDa was not significant. Contrast-enhanced MRI is effective for noninvasive real-time visualization of in vivo drug delivery of paramagnetically labeled polymer conjugates.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 8

IT 912576-20-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(noninvasive visualization of in vivo drug delivery of poly(L-glutamic acid) using contrast-enhanced MRI)

IT 22541-19-1, Gd3+, biological studies 912576-20-6D, reaction products with polyglutamic acid, gadolinium complexes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(noninvasive visualization of in vivo drug delivery of poly(L-glutamic acid) using contrast-enhanced MRI)

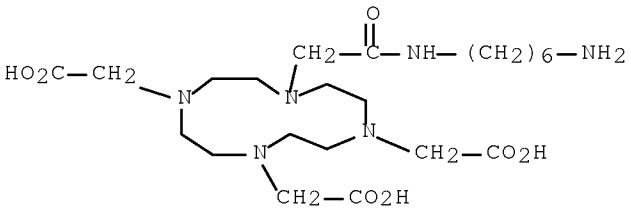
IT 912576-20-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(noninvasive visualization of in vivo drug delivery of poly(L-glutamic acid) using contrast-enhanced MRI)

RN 912576-20-6 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-aminohexyl)amino]-2-oxoethyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

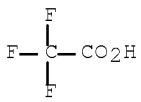
CM 1

CRN 889140-15-2
CMF C22 H42 N6 O7



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(noninvasive visualization of in vivo drug delivery of poly(L-glutamic

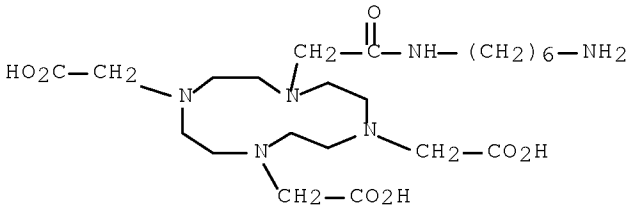
acid) using contrast-enhanced MRI
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 12 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:836023 ZCAPLUS Full-text
DOCUMENT NUMBER: 147:26007
TITLE: Biodegradable cystamine spacer facilitates the clearance of Gd(III) chelates in poly(glutamic acid) Gd-DO3A conjugates for contrast-enhanced MR imaging
AUTHOR(S): Ke, Tianyi; Feng, Yi; Guo, Junyu; Parker, Dennis L.; Lu, Zheng-Rong
CORPORATE SOURCE: Department of Pharmaceutics and Pharmaceutical Chemistry, University of Utah, Salt Lake City, UT, 84108, USA
SOURCE: Magnetic Resonance Imaging (2006), 24(7), 931-940
CODEN: MRIMDQ; ISSN: 0730-725X
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Poly(-glutamic acid) (PGA)-cystamine-[gadolinium (Gd)-DO3A] was prepared in high yield with a high Gd-DO3A conjugation efficiency. Approx. 55% of the carboxylic groups in PGA were loaded with Gd-DO3A via cystamine as the spacer. Cystamine can be readily cleaved by endogenous thiols to release the Gd(III) chelates from the conjugate facilitating Gd(III) excretion after the magnetic resonance imaging (MRI). The contrast-enhanced MRI with PGA-cystamine-(Gd-DO3A) was investigated in mice bearing MDA-MB-231 breast carcinoma xenografts. PGA-1,6-hexanediamine-(Gd-DO3A), a paramagnetic polymer conjugate of a nondegradable spacer, was used as a control. Both conjugates resulted in similar contrast enhancement in the heart, vasculature, liver and kidneys in the first hour post injection. More substantial signal intensity reduction was observed for PGA-cystamine-(Gd- DO3A) in these organs than PGA-1,6-hexanediamine-(Gd-DO3A) due to release of the Gd chelates from PGA-cystamine-(Gd-DO3A) after the cleavage of the disulfide spacer by the endogenous thiols. Both conjugates resulted in similar tumor enhancement with approx. 70% increased signal intensity in the tumor periphery and 10-40% increased signal intensity in tumor interstitium. No cross-reaction was observed between PGA-cystamine-(Gd-DO3A) and human serum albumin, a plasma protein containing a cysteine residue. PGA-cystamine-(Gd-DO3A) resulted in significantly lower Gd(III) tissue retention than PGA-1,6-hexanediamine-(Gd-DO3A) 10 days after the injection in the mice ($P<.05$). The conjugation of Gd(III) chelates to biomedical copolymers via the degradable disulfide spacer resulted in significant contrast enhancement in the blood pool and tumor tissue but minimal long-term Gd(III) tissue retention.
CC 8-9 (Radiation Biochemistry)
IT Imaging
(tumor; role of biodegradable cystamine spacer in clearance of Gd(III)chelates in poly(glutamic acid)Gd-DO3A conjugates for contrast enhanced magnetic resonance imaging of breast carcinomas)
IT 25513-46-6DP, reaction products with acetic acid tetraazacyclododecane cystamine derivs. 585531-76-6DP, polyglutamic acid derivs., gadolinium complexes 889140-15-2DP, polyglutamic acid derivs., gadolinium complexes
RL: PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(role of biodegradable cystamine spacer in clearance of Gd(III)chelates in poly(glutamic acid)Gd-DO3A conjugates for contrast enhanced magnetic resonance imaging of breast carcinomas)
IT 114873-37-9P 122555-91-3P 485800-28-0P 585531-76-6P 889140-15-2P 938041-81-7P

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(role of biodegradable cystamine spacer in clearance of Gd(III)chelates in poly(glutamic acid)Gd-DO3A conjugates for contrast enhanced magnetic resonance imaging of breast carcinomas)

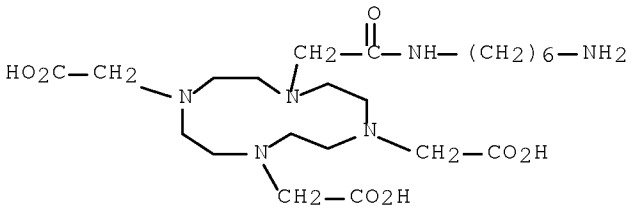
IT 889140-15-2DP, polyglutamic acid derivs., gadolinium complexes
RL: PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(role of biodegradable cystamine spacer in clearance of Gd(III)chelates in poly(glutamic acid)Gd-DO3A conjugates for contrast enhanced magnetic resonance imaging of breast carcinomas)

RN 889140-15-2 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-aminohexyl)amino]-2-oxoethyl]- (CA INDEX NAME)



IT 889140-15-2P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(role of biodegradable cystamine spacer in clearance of Gd(III)chelates in poly(glutamic acid)Gd-DO3A conjugates for contrast enhanced magnetic resonance imaging of breast carcinomas)

RN 889140-15-2 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-aminohexyl)amino]-2-oxoethyl]- (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 13 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:779890 ZCAPLUS Full-text
DOCUMENT NUMBER: 145:391420
TITLE: Structure-Activity Relationships of 111In- and 99mTc-Labeled Quinolin-4-one Peptidomimetics as Ligands for the Vitronectin Receptor: Potential Tumor Imaging Agents

AUTHOR(S): Harris, Thomas D.; Kalogeropoulos, Shirley; Nguyen, Tiffany; Dwyer, Gregory; Edwards, D. Scott; Liu, Shuang; Bartis, Judit; Ellars, Charles; Onthank, Dave; Yalamanchili, Padmaja; Heminway, Stuart; Robinson, Simon; Lazewatsky, Joel; Barrett, John
CORPORATE SOURCE: Discovery Research, Bristol-Myers Squibb Medical Imaging, N. Billerica, MA, 01862, USA
SOURCE: Bioconjugate Chemistry (2006), 17(5), 1294-1313
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The integrin receptor αvβ3 is overexpressed on the endothelial cells of growing tumors and on some tumor cells themselves. Radiolabeled αvβ3 antagonists have demonstrated potential application as tumor imaging agents and as radiotherapeutic agents. This report describes the total synthesis of eight new HYNIC and DOTA conjugates of receptor αvβ3 antagonists belonging to the quinolin-4-one class of peptidomimetics, and their radiolabeling with 99mTc (for HYNIC) and 111In (for DOTA). Tethering of the radionuclide-chelator complexes was achieved at two different sites on the quinolin-4-one mol. All such derivs. maintained high affinity for receptor αvβ3 and high selectivity vs. receptors αIIbβ3, αvβ5, α5β1. Biodistribution of the radiolabeled compds. was evaluated in the c-neu Oncomouse mammary adenocarcinoma model. DOTA conjugate 111In-TA138 presented the best biodistribution profile. Tumor uptake at 2 h postinjection was 9.39% of injected dose/g of tissue (%ID/g). Activity levels in selected organs was as follows: blood, 0.54% ID/g; liver, 1.94% ID/g; kidney, 2.33% ID/g; lung, 2.74% ID/g; bone, 1.56% ID/g. A complete biodistribution anal. of 111In-TA138 and the other radiolabeled compds. of this study are presented and discussed. A scintigraphic imaging study with 111In-TA138 showed a clear delineation of the tumors and rapid clearance of activity from nontarget tissues.

CC 8-9 (Radiation Biochemistry)
ST prepn radiolabeled quinolinone peptidomimetic vitronectin receptor tumor imaging
IT Scintigraphic agents
Scintigraphy
Structure-activity relationship
(SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)
IT Vitronectin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)
IT Mammary gland, neoplasm
(adenocarcinoma; SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)
IT Carcinoma
(mammary adenocarcinoma; SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)
IT Pharmacokinetics
(organ uptake; SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)
IT Imaging
(tumor; SAR and preparation of 111In- and 99mTc-labeled

quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αIIbβ3; SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αvβ3; SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αvβ5; SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α5β1; SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)

IT 15750-15-9DP, Indium 111, conjugates, biological studies 278172-91-1P 278172-95-5P 278172-98-8P 278172-99-9P 378784-45-3DP, Technetium 99m, conjugates, biological studies 498575-44-3DP, technetium-99 complex 498575-49-8DP, technetium-99 complex 498575-53-4DP, technetium-99 complex 911209-04-6P
RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)

IT 501-53-1 3406-84-6, Biphenyl-4,4'-disulfonyl chloride 4246-51-9 7790-94-5, Chlorosulfonic acid 66414-73-1 72080-83-2, Benzyl N-(2-aminoethyl)carbamate 77087-60-6 83948-53-2 98541-64-1 114559-25-0 137076-54-1, DOTA tri(tert-butyl) ester 185563-93-3 206055-18-7 208580-23-8 208580-27-2 277315-96-5 277316-23-1 277316-26-4 277316-29-7 848083-49-8 911141-44-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)

IT 40324-66-1P 57932-18-0P 220156-99-0P 250612-31-8P 277315-53-4P 277315-71-6P 277315-77-2P 277315-83-0P 277315-84-1P 277315-85-2P 277315-86-3P 277315-87-4P 277315-89-6P 277315-90-9P 277315-97-6P 277315-98-7P 277315-99-8P 277316-00-4P 277316-01-5P 277316-02-6P 277316-03-7P 277316-09-3P 277316-10-6P 277316-11-7P 277316-24-2P 277316-28-6P 277316-40-2P 277316-41-3P 277316-42-4P 277316-43-5P 277316-46-8P 277316-50-4P 277316-51-5P 277316-58-2P 498575-82-9P 498575-84-1P 498575-86-3P 569328-06-9P 911141-43-0P 911141-45-2P 911141-46-3P 911141-47-4P 911141-48-5P 911141-49-6P 911141-50-9P 911141-52-1P 911141-53-2P 911141-54-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)

IT 911141-45-2DP, technetium-99 complex 911141-55-4P 911141-56-5P
RL: SPN (Synthetic preparation); PREP (Preparation)

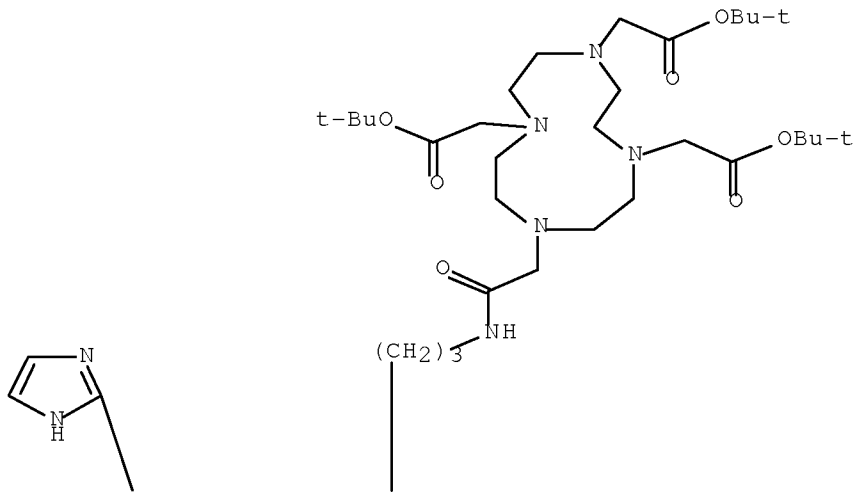
(SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)

IT 277316-46-8P 911141-54-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(SAR and preparation of 111In- and 99mTc-labeled quinolin-4-one peptidomimetics as ligands for vitronectin receptor and potential tumor imaging agents)

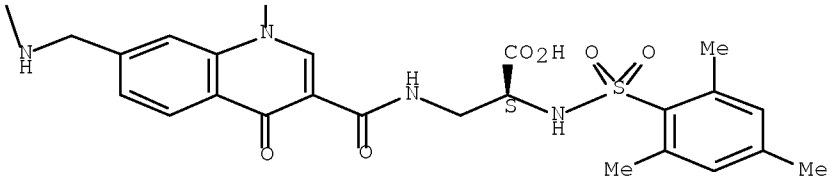
RN 277316-46-8 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-oxoethyl]-, α,α',α''-tris(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



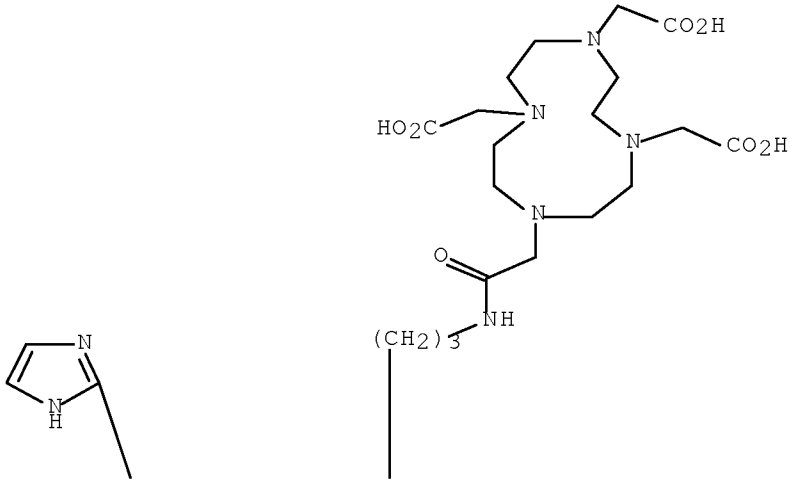
RN 911141-54-3 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[3-[[[(2S)-2-carboxy-2-[[(2,4,6-trimethylphenyl)sulfonyl]amino]ethyl]amino]carbonyl]-7-[(1H-imidazol-2-ylamino)methyl]-4-oxo-1(4H)-quinolinyl]propyl]amino]-2-oxoethyl]-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

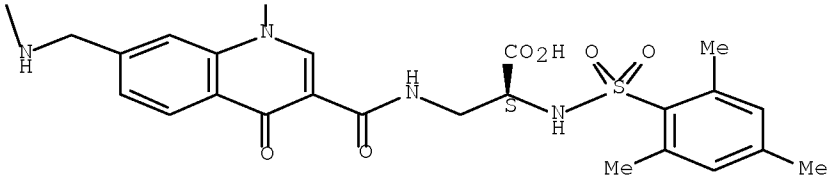
CRN 277315-74-9
CMF C45 H61 N11 O13 S

Absolute stereochemistry.

PAGE 1-A

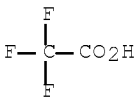


PAGE 2-A



CM 2

CRN 76-05-1
CMF C2 H F3 O2



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 14 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:681369 ZCAPLUS Full-text
DOCUMENT NUMBER: 145:146029
TITLE: Preparation of peptide-containing compounds for targeting cells expressing NP-1 receptor
INVENTOR(S): Von Wronski, Mathew A.; Marinelli, Edmund R.; Nunn, Adrian D.; Pillai, Radhakrishna; Ramalingam, Kondareddiar; Tweedle, Michael F.; Linder, Karen E.; Nanjappan, Palaniappa; Raju, Natarajan
PATENT ASSIGNEE(S): Bracco International B.V., Neth.
SOURCE: U.S. Pat. Appl. Publ., 98 pp., Cont.-in-part of Ser. No. US 2001-871974,
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006153775	A1	20060713	US 2006-342050	20060127
US 2002147136	A1	20021010	US 2001-871974	20010604
US 7109167	B2	20060919		
WO 2007090022	A2	20070809	WO 2007-US61019	20070125
WO 2007090022	A3	20071122		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2000-585364 B2 20000602
US 2001-871974 A2 20010604
US 2006-342050 A 20060127

OTHER SOURCE(S): MARPAT 145:146029

AB The invention provides compds. for targeting endothelial cells, tumor cells or other cells that express the neuropilin-1 (NP-1) receptor, compns. containing the same and methods for their use. The compds. are of the formula A-L-B (A = a monomer, multimer or polymer of TKPPR or analog which specifically binds to NP-1 or cells expressing NP-1 with avidity equal or greater than TKPPR; L = a lipid or a non-lipid (e.g., polymer) linker; B = a substrate). Addnl., the present invention includes diagnostic, therapeutic and radio-therapeutic compns. useful for visualization, therapy or radiotherapy. For example, DPPE-glutaroyl-Gly-Thr-Lys-Pro-Pro- Arg-OH (DPPE-Glu-GTKPPR) was prepared and formulated into gas-filled microbubble compns. for ultrasonic echog. The bubbles bind to human aortic endothelial cells (HAEC) under flow. The number of bubbles bound may increase with time for several minutes at a given flow rate, up to a flow rate producing 1.53 dynes/cm2, while bubbles without the targeting moiety (DPPE-Glu-GTKPPR) may not bind. However, once bound under a lesser flow rate (e.g., 1.53 dynes/cm2), the shear stress on bubbles

containing DPPE-Glu-GTKPPR may be increased to 6.1 dynes/cm2 without dislodging many of the bound bubbles.

INCL 424009340; 530326000

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1, 8, 63

ST peptide neuropilin receptor endothelium tumor targeting; antitumor angiogenesis inhibitor peptide deriv prepn; gene therapy radiotherapy peptide deriv; ultrasound imaging endothelium neuropilin peptide

IT Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(human aortic endothelial cells activated by; preparation of peptide-containing
compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)

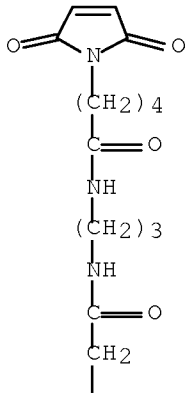
IT 100-46-9, Benzenemethanamine, reactions 1155-64-2 1663-39-4 4530-20-5 5681-36-7 7672-27-7 15401-08-8 29022-11-5 33662-26-9 71989-26-9 71989-35-0 76931-93-6 82911-69-1 106392-12-5 120791-76-6 129223-22-9 166108-71-0 167393-62-6 169543-81-1 198139-51-4 251450-64-3 283176-26-1 377087-81-5D, resin bound 377087-83-7D, resin-bound 470444-40-7 897930-81-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptide-containing compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)

IT 897930-81-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptide-containing compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)

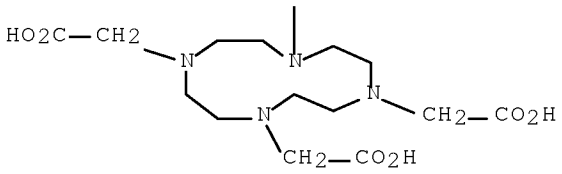
RN 897930-81-3 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[[5-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopentyl]amino]propyl]amino]-2-oxoethyl]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L80 ANSWER 15 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:542454 ZCAPLUS Full-text
DOCUMENT NUMBER: 145:34213
TITLE: MRI-guided photodynamic therapy for cancer
INVENTOR(S): Lu, Zheng-Rong; Viadya, Anagha; Ke, Tianyi
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060797	A2	20060608	WO 2005-US44012	20051202
WO 2006060797	A3	20060824		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005311560	A1	20060608	AU 2005-311560	20051202
CA 2589881	A1	20060608	CA 2005-2589881	20051202
EP 1830879	A2	20070912	EP 2005-853048	20051202
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
KR 2007086803	A	20070827	KR 2007-714910	20070629
PRIORITY APPLN. INFO.:			US 2004-633255P P	20041203
			WO 2005-US44012 W	20051202

AB Disclosed is a method of therapy used in combination with a diagnostic tool for enhanced photodynamic therapy using MRI, called (magnetic resonance imaging)-guided photodynamic therapy. The methods of the present invention include administration of MRI contrast agent-labeled polymer photosensitizer conjugates, detection and localization of tumor or cancer tissues with contrast-enhanced MRI and specific illumination and treatment of localized target tissues, such as tumors or cancer cells, using laser energy. The delivered laser energy activates the photosensitizer accumulated in the target tissue, resulting in treatment. Also disclosed are novel conjugate compds., such as PLGA-Mce6-DOTA-Gd complexes, having multi-functionality in that the

complex may include an MRI contrasting agent linked to a photosensitizing agent.

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 8

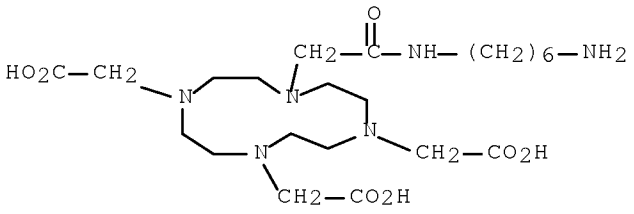
ST polyglutamate photosensitizer MRI contrast agent delivery tumor; photodynamic therapy MRI imaging breast cancer

IT Antitumor agents
Human
Neoplasm
Photodynamic therapy
Photosensitizers, pharmaceutical
(delivery systems for MRI-guided photodynamic therapy of cancer)

IT 668-74-6DP, reaction products with polyglutamic acids and DOTA, gadolinium complexes 7440-54-2DP, Gadolinium, reaction products with polyglutamic acids, DOTA, and Mce6 25014-27-1DP, deprotected, pyrrolidone esters, DOTA/porphine gadolinium complexes 25038-53-3DP, deprotected, pyrrolidone esters, DOTA/porphine derivs., gadolinium complexes 889140-15-2DP, reaction products with polyglutamic acids, gadolinium complexes
RL: DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(delivery systems for MRI-guided photodynamic therapy of cancer)

IT 889140-15-2DP, reaction products with polyglutamic acids, gadolinium complexes
RL: DGN (Diagnostic use); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(delivery systems for MRI-guided photodynamic therapy of cancer)

RN 889140-15-2 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-aminohexyl)amino]-2-oxoethyl]- (CA INDEX NAME)



L80 ANSWER 16 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:343390 ZCAPLUS Full-text
DOCUMENT NUMBER: 144:398254
TITLE: Targeted imaging and/or therapy using the Staudinger ligation
INVENTOR(S): Robillard, Marc S.; Gruell, Holger
PATENT ASSIGNEE(S): Koninklijke Philips Electronics N.V., Neth.
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006038185	A2	20060413	WO 2005-IB53258	20051004
WO 2006038185	A3	20060713		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1799273	A2	20070627	EP 2005-788346	20051004
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101068577	A	20071107	CN 2005-80034471	20051004
IN 2007CN01400	A	20070831	IN 2007-CN1400	20070405
PRIORITY APPLN. INFO.:			EP 2004-104913 A	20041007
			WO 2005-IB53258 W	20051004

OTHER SOURCE(S): MARPAT 144:398254

AB The use of a selective chemical and bioorthogonal reaction providing a covalent ligation such as the Staudinger ligation (reaction between an azide and a phosphine), in targeted mol. imaging and therapy is presented, more specifically with interesting applications for pre-targeted imaging or therapy. Current pre-targeted imaging is hampered by the fact that it relies solely on natural/biol. targeting constructs (i.e. biotin/streptavidin). Size considerations and limitations associated with their endogenous nature severely limit the number of applications. The present invention describes how the use of an abiotic, bio-orthogonal reaction which forms a stable adduct under physiol. conditions, by way of a small or undetectable bond, can overcome these limitations. As an example of pre-targeted imaging, injection of a targeting probe comprising a somatostatin receptor-binding peptide linked to an azide is followed by a secondary radiolabeled probe linked to a Staudinger phosphine group. Following in vivo Staudinger ligation, the radiolabel enables detection of the presence of somatostatin receptor-pos. tissue such as neuroendocrine tumor.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 8, 21

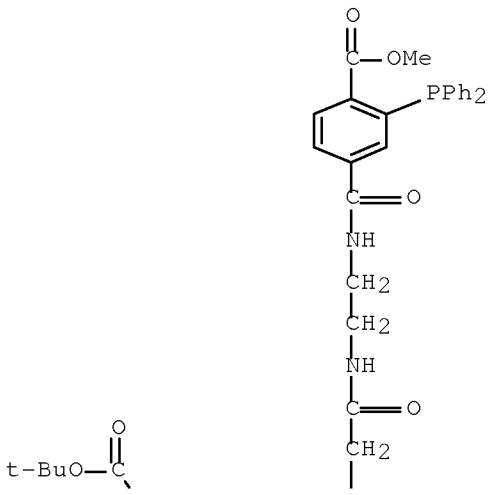
IT 57260-73-8P 137076-54-1P 149299-82-1P 153086-78-3P 175854-39-4P 192635-89-5P 251564-45-1P 299173-24-3P 361154-31-6P 726698-17-5P 868394-26-7P 882518-79-8P 882518-80-1P 882518-81-2P 882518-82-3P 882518-83-4P 882518-85-6P 882518-86-7P 882518-88-9P 882518-89-0P 882518-90-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(targeted imaging and/or therapy using Staudinger ligation)

IT 882518-83-4P 882518-85-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(targeted imaging and/or therapy using Staudinger ligation)

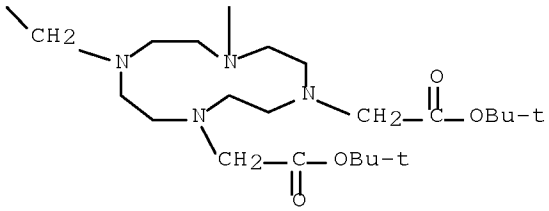
RN 882518-83-4 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[3-(diphenylphosphino)-4-(methoxycarbonyl)benzoyl]amino]ethyl]amino]-2-oxoethyl]-, tris(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

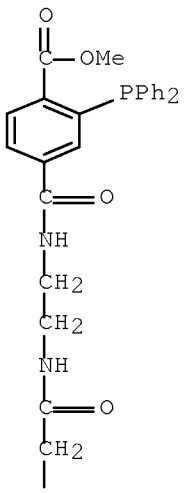


RN 882518-85-6 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[3-(diphenylphosphino)-4-(methoxycarbonyl)benzoyl]amino]ethyl]amino]-2-oxoethyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

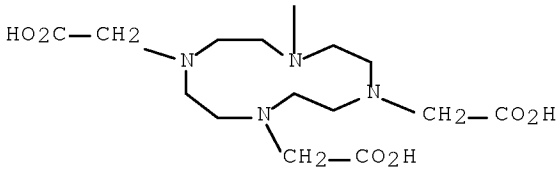
CM 1

CRN 882518-84-5
CMF C39 H49 N6 O10 P

PAGE 1-A

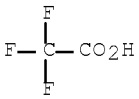


PAGE 2-A



CM 2

CRN 76-05-1
CMF C2 H F3 O2



L80 ANSWER 17 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:79358 ZCAPLUS Full-text
DOCUMENT NUMBER: 144:156642
TITLE: Compositions and methods for treating cancer
INVENTOR(S): Mayers, George, L.; Lee, David; Chin, Hsiao Ling
PATENT ASSIGNEE(S): Oncologic, Inc., USA
SOURCE: PCT Int. Appl., 111 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006010165	A2	20060126	WO 2005-US26248	20050725
WO 2006010165	A3	20070208		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006018908	A1	20060126	US 2004-897530	20040723
AU 2005265425	A1	20060126	AU 2005-265425	20050725
CA 2572825	A1	20060126	CA 2005-2572825	20050725
EP 1809332	A2	20070725	EP 2005-802465	20050725
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				

PRIORITY APPLN. INFO.:
US 2004-897530 A 20040723
WO 2005-US26248 W 20050725

AB The invention features compns. and methods for treating or alleviating a symptom of cancer. The compns. and methods of the invention direct supra-LDs of radiation, called Hot-Spots, to virtually all cancer cell types. Cancer is treated by administering a step 1 reagent containing a cell-targeting agent linked to a platform building material; a step 3 reagent containing a targeting moiety and an isotope trapping moiety; and a radiolabeled aqueous soluble set 4 reagent. The cell targeting agent augments cellular uptake of the step 1 reagent. The platform building material detaches from the cell targeting agent upon uptake of the step 1 reagent into the cell and forms an aqueous insol. nano-platform to which the targeting moiety of the step 3 reagent binds. Optionally, a step 2 cell-killing reagent is administered to the subject prior to, after or concurrently with the step 3 reagent to relocate the nano-platform into the tumor extracellular matrix. An example of an agent is an anti-EGF-antibody- dextran-3-indoxyl phosphate-phosphoenol pyruvate conjugate.

CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 8, 15

IT Drug delivery systems
(carriers; radiolabeled tumor-targeted antibody carrier conjugates)

IT Antibodies and Immunoglobulins
Galactosides
Glycosides
Porphyrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates; radiolabeled tumor-targeted antibody carrier conjugates)

IT Glycosides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(glucuronides, conjugates; radiolabeled tumor-targeted antibody carrier conjugates)
IT Drug delivery systems
(immunoconjugates; radiolabeled tumor-targeted antibody carrier conjugates)
IT Drug delivery systems
(immunotoxins; radiolabeled tumor-targeted antibody carrier conjugates)
IT Antitumor agents
Human
Radiopharmaceuticals
(radiolabeled tumor-targeted antibody carrier conjugates)
IT Albumins, biological studies
Antibodies and Immunoglobulins
Lactams
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radiolabeled tumor-targeted antibody carrier conjugates)
IT 62229-50-9, Egf
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibodies to, conjugates; radiolabeled tumor-targeted antibody carrier conjugates)
IT 9024-60-6, Ornithine decarboxylase 9024-77-5, Arginine decarboxylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; radiolabeled tumor-targeted antibody carrier conjugates)
IT 9073-60-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(radiolabeled tumor-targeted antibody carrier conjugates)
IT 104-87-0 109-97-7, Pyrrol 119-24-4 122-85-0 616-34-2 619-44-3
619-66-9 874-60-2 2646-51-7 3068-32-4 4203-49-0 16522-41-1
21442-01-3 30924-93-7 37293-51-9, Aminodextran 38862-25-8
58626-38-3 60239-18-1, Dota 63379-64-6 76470-66-1, Loracarbef
76931-93-6 88738-51-6 89992-70-1 102262-50-0 109448-27-3
115416-38-1 125878-06-0 220935-13-7 236404-46-9 874201-16-8
874201-25-9 874201-26-0 874201-36-2 874201-81-7 874201-87-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(radiolabeled tumor-targeted antibody carrier conjugates)
IT 61449-63-6P 64244-53-7P 66646-88-6P 78658-49-8P 147804-55-5P
214554-43-5P 214554-44-6P 266341-16-6P 266341-19-9P 623907-52-8P
762241-39-4P 847944-61-0P 847944-62-1P 847944-63-2P 874201-13-5P
874201-14-6P 874201-15-7P 874201-17-9P 874201-18-0P 874201-19-1P
874201-20-4P 874201-21-5P 874201-22-6P 874201-23-7P 874201-24-8P
874201-27-1P 874201-28-2P 874201-29-3P 874201-30-6P 874201-31-7P
874201-32-8P 874201-33-9P 874201-34-0P 874201-35-1P 874201-37-3P
874201-39-5P 874201-40-8P 874201-41-9P 874201-42-0P 874201-43-1P
874201-44-2P 874201-45-3P 874201-46-4P 874201-47-5P 874201-48-6P
874201-49-7P 874201-51-1P 874201-53-3P 874201-55-5P 874201-59-9P
874201-61-3P 874201-64-6P 874201-65-7P 874201-66-8P 874201-67-9P
874201-68-0P 874201-69-1P 874201-71-5P 874201-73-7P 874201-75-9P
874201-77-1P 874201-81-7DP, conjugates with polymer 874201-83-9P
874201-84-0P 874201-85-1P 874201-86-2P 874201-88-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(radiolabeled tumor-targeted antibody carrier conjugates)
IT 59-30-3DP, Folic acid, conjugates 9013-20-1DP, Streptavidin, conjugates
9023-27-2DP, UDP-N-acetylglucosamine enolpyruvyltransferase, conjugates
10098-91-6DP, Yttrium 90, conjugated complexes, biological studies
21442-01-3DP, polymer conjugated derivs. 847944-66-5DP, yttrium 90 complexes 847944-67-6P 847944-68-7P 847944-69-8P 847944-70-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological

study); PREP (Preparation); USES (Uses)
(radiolabeled tumor-targeted antibody carrier conjugates)

IT 138-08-9D, Phosphoenol pyruvic acid, conjugated derivs. 619-66-9D, 4-Carboxybenzaldehyde, conjugates 9001-78-9D, conjugates 9004-54-0D, Dextran, conjugated derivs. 9031-11-2D, conjugates 13822-19-0D, 3-Indoxyl phosphate, conjugated derivs. 70052-12-9D, α-Difluoromethylornithine, conjugated derivs. 724705-43-5D, Carbacephem, conjugated derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radiolabeled tumor-targeted antibody carrier conjugates)

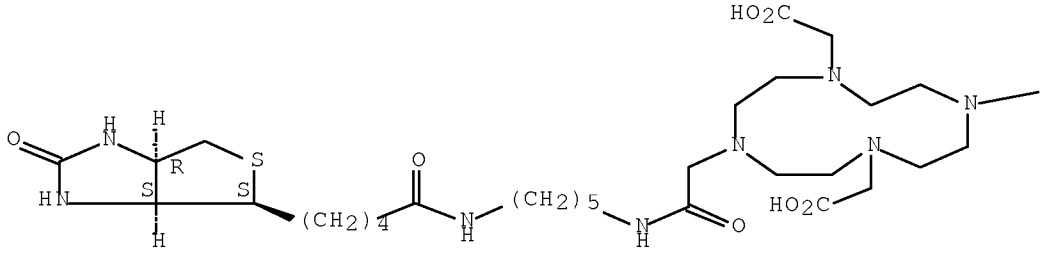
IT 847944-66-5DP, yttrium 90 complexes
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(radiolabeled tumor-targeted antibody carrier conjugates)

RN 847944-66-5 ZCAPLUS

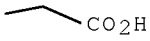
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[5-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]pentyl]amino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L80 ANSWER 18 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:79312 ZCAPLUS Full-text

DOCUMENT NUMBER: 144:171259

TITLE: Preparation of gastrin-releasing peptide compounds for use in diagnostic imaging or therapy

INVENTOR(S): Cappelletti, Enrico; Lattuada, Luciano; Linder, Karen E.; Marinelli, Edmund; Nanjappan, Palaniappa; Raju, Natarajan; Ramalingam, Kondareddiar; Swenson, Rolf E.; Tweedle, Michael

PATENT ASSIGNEE(S): Bracco Imaging S.p.A., Italy

SOURCE: U.S. Pat. Appl. Publ., 194 pp., Cont.-in-part of U.S. Ser. No. 828,925.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006018830	A1	20060126	US 2005-165721	20050624
US 2004136906	A1	20040715	US 2003-341577	20030113
US 7226577	B2	20070605		
WO 2004065407	A2	20040805	WO 2003-US41328	20031224
WO 2004065407	A3	20040923		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004253225	A1	20041216	US 2004-828925	20040420
US 2006239914	A1	20061026	US 2006-352156	20060210
WO 2007002500	A1	20070104	WO 2006-US24641	20060623
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
IN 2006CN02330	A	20070706	IN 2006-CN2330	20060626
US 2008008649	A1	20080110	US 2007-751337	20070521
PRIORITY APPLN. INFO.:			US 2003-341577	A2 20030113
			WO 2003-US41328	A2 20031224
			US 2004-828925	A2 20040420
			WO 2004-US22115	W 20040712
			US 2005-165721	A2 20050624
			US 2006-352156	A2 20060210
OTHER SOURCE(S):	MARPAT 144:171259			

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to compds. M-N-O-P-G (M is a metal chelator, preferably an Aazta metal chelator or a derivative; N-O-P is a linker containing at least one non-α-amino acid and at least one substituted bile acid; G is the GRP receptor targeting peptide) for use in diagnostic imaging, radiotherapy or phototherapy. Thus, peptide I was prepared and its complex with 177Lu was evaluated for tumor targeting capacity, biodistribution and kinetics in the human PC-3 nude mouse model.

INCL 424001690; 514183000; 534011000
CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 8, 78

IT 55749-98-9P 55749-99-0P 87096-84-2P, Neuromedin B (swine spinal cord)
422512-72-9P 422512-75-2P 422512-81-0P 721936-47-6P 721936-49-8P
721936-51-2P 721936-53-4P 721936-55-6P 721936-57-8P 721936-59-0P
721936-61-4P 721936-63-6P 721936-67-0P 721936-69-2P 721936-71-6P
721936-73-8P 721936-75-0P 721936-76-1P 721936-78-3P 721936-80-7P
721936-82-9P 721936-92-1P 721936-94-3P 721936-96-5P 721936-98-7P
721936-99-8P 721937-01-5P 721937-03-7P 721937-05-9P 721937-07-1P
721937-09-3P 721937-11-7P 721937-13-9P 721937-15-1P 721937-17-3P
721937-19-5P 721937-21-9P 721937-23-1P 721937-25-3P 721937-27-5P
721937-29-7P 721937-31-1P 721937-33-3P 721937-35-5P 721937-37-7P
721937-40-2P 721937-42-4P 721937-44-6P 721937-46-8P 721937-48-0P
721937-50-4P 721937-52-6P 721937-54-8P 721937-56-0P 721937-58-2P
721937-60-6P 721937-62-8P 721937-64-0P 721937-66-2P 721937-68-4P
721937-70-8P 721937-72-0P 721937-74-2P 721937-76-4P 721937-78-6P
721937-80-0P 721937-82-2P 721937-84-4P 721937-86-6P
721937-88-8P 721937-90-2P 721937-92-4P 721937-94-6P
721937-96-8P 721937-98-0P 721938-00-7P 721938-02-9P 721938-04-1P
721938-06-3P 721938-08-5P 721938-10-9P 721938-12-1P 721938-14-3P
721938-16-5P 721938-18-7P 721938-20-1P 721938-22-3P 721938-24-5P
721938-26-7P 721938-28-9P 721938-30-3P 721938-32-5P 721938-34-7P
721938-36-9P 721938-38-1P 721938-39-2P 721938-41-6P 721938-43-8P
721938-45-0P 721938-47-2P 721938-49-4P 721938-51-8P 721938-54-1P
721938-56-3P 721938-58-5P 721938-60-9P 721938-62-1P 721938-64-3P
721938-66-5P 721938-68-7P 721938-70-1P 721938-72-3P 721938-74-5P
721938-76-7P 721938-78-9P 721938-80-3P 721938-83-6P 721938-85-8P
721938-87-0P 721938-89-2P 721938-97-2P 721938-99-4P 721939-01-1P
721939-03-3P 721939-05-5P 721939-06-6P 721939-07-7P 721939-08-8P
721939-10-2P 721939-11-3P 721939-12-4P 721939-14-6P 721939-16-8P
721939-17-9P 721939-18-0P 721939-19-1P 721939-21-5P 721939-23-7P
721939-25-9P 721939-27-1P 721939-29-3P 721939-31-7P 721939-33-9P
721939-35-1P 721939-37-3P 722493-92-7P 722493-93-8P 722493-94-9P
722493-95-0P 722493-96-1P 722493-97-2P 722493-98-3P 722493-99-4P
722494-00-0P 722494-01-1P 722494-02-2P 808112-30-3P 808112-31-4P
808112-32-5P 808112-33-6P 808112-35-8P 808112-37-0P 808112-39-2P
808112-41-6P 808112-43-8P 808112-44-9P 808112-45-0P
808112-46-1P 808112-47-2P 808112-48-3P 808112-49-4P 808112-50-7P
808112-51-8P 808112-52-9P 808112-53-0P 808112-54-1P 808112-55-2P
808112-56-3P 808112-57-4P 808112-58-5P 808112-59-6P 808112-60-9P
808112-61-0P 808112-62-1P 808112-63-2P 808112-64-3P 808112-65-4P
808112-67-6P 808112-68-7P 808112-69-8P 808112-70-1P 808112-71-2P
808112-72-3P 808112-73-4P 808112-74-5P 808112-75-6P
808112-76-7P 808113-00-0P 808113-01-1P 808113-02-2P 808113-03-3P
808113-04-4P 808113-05-5P 808113-06-6P 808113-07-7P 808113-08-8P
808113-09-9P 808113-10-2P 808113-11-3P 808113-12-4P 808113-14-6P
809233-13-4P 874367-58-5P 874534-72-2P 874534-73-3P 874537-63-0P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of gastrin-releasing peptide compds. for use in diagnostic imaging or therapy)

IT 721937-82-2P 721937-90-2P 721937-92-4P
808112-41-6P 808112-74-5P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of gastrin-releasing peptide compds. for use in diagnostic imaging or therapy)

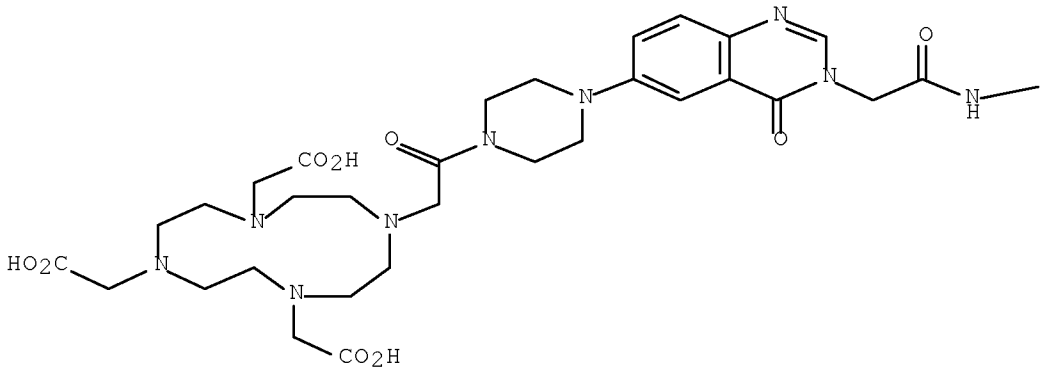
RN 721937-82-2 ZCAPLUS

CN L-Methioninamide, N2-[[4-oxo-6-[4-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-1-piperazinyl]-3(4H)-quinazolinyl]acetyl]-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl-

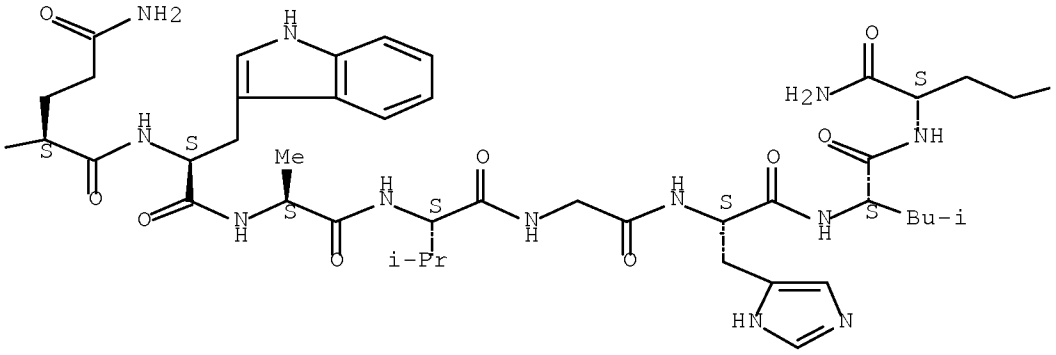
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



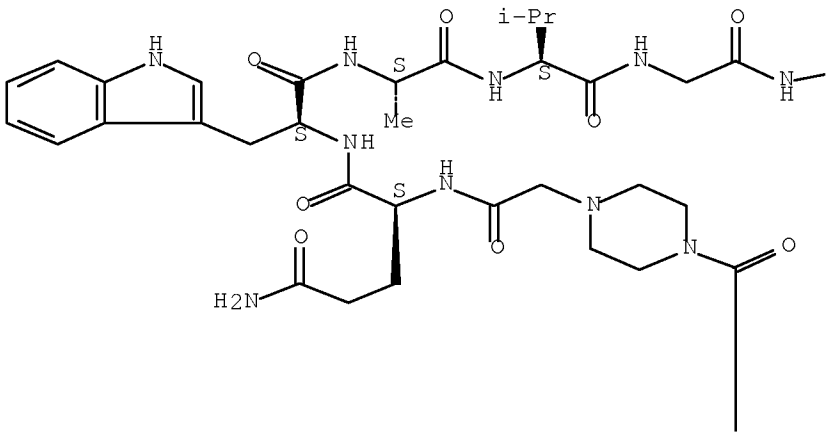
PAGE 1-C

RN 721937-90-2 ZCAPLUS

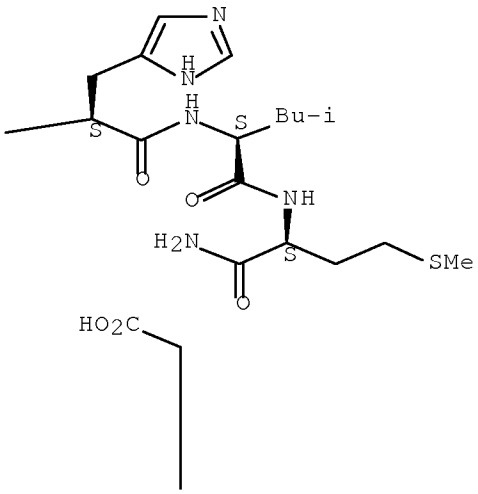
CN L-Methioninamide, N2-[[4-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-1-piperazinyl]acetyl]-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

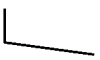
PAGE 1-A



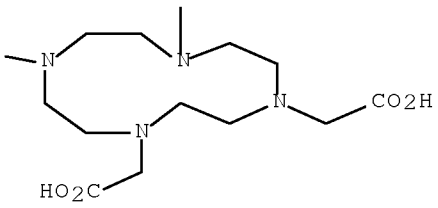
PAGE 1-B



PAGE 2-A



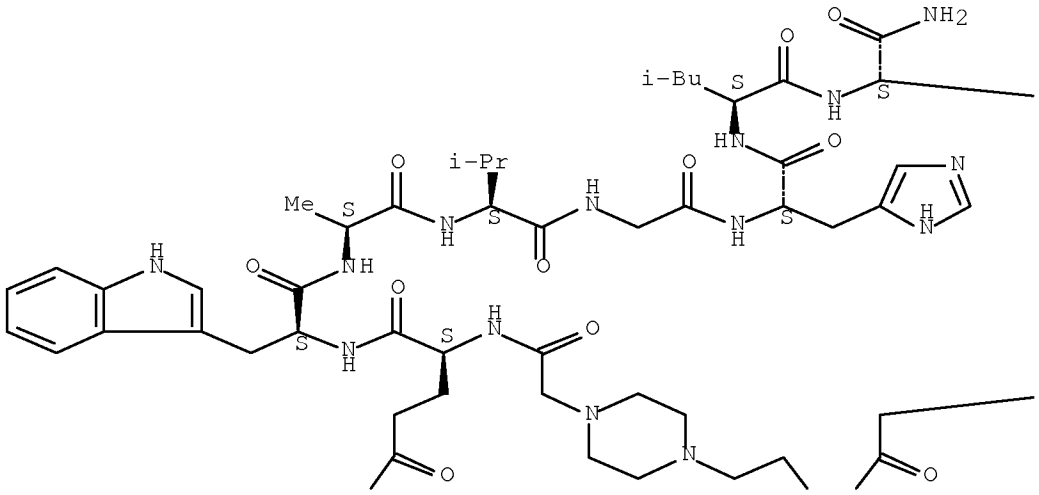
PAGE 2-B



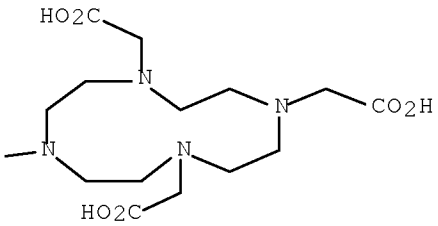
RN 721937-92-4 ZCAPLUS
CN L-Methioninamide, N2-[[4-[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]-1-piperazinyl]acetyl]-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

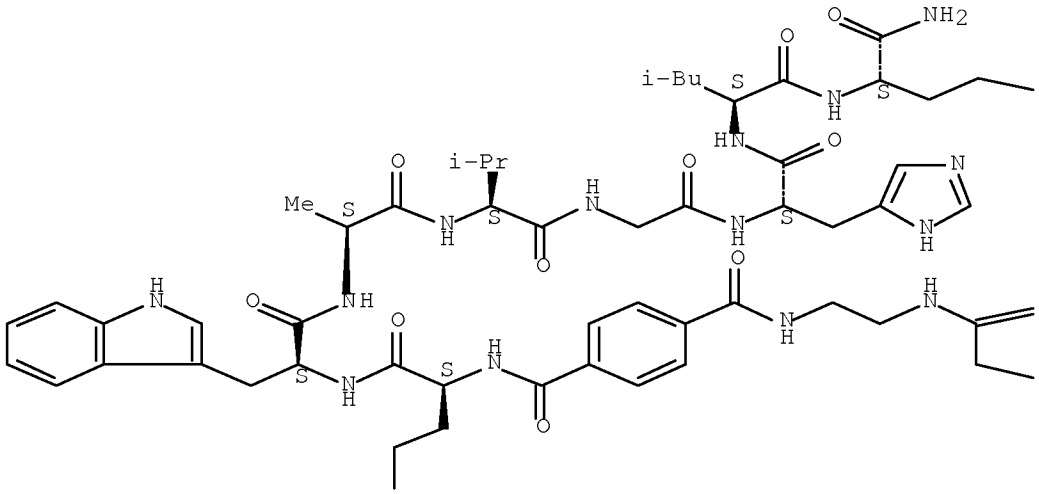


PAGE 2-A

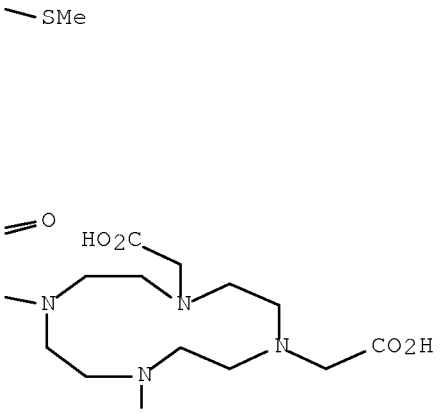
RN 808112-41-6 ZCAPLUS
CN L-Methioninamide, N2-[4-[[[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]carbonyl]benzoyl]-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

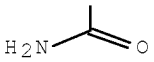
PAGE 1-A



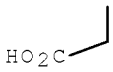
PAGE 1-B



PAGE 2-A



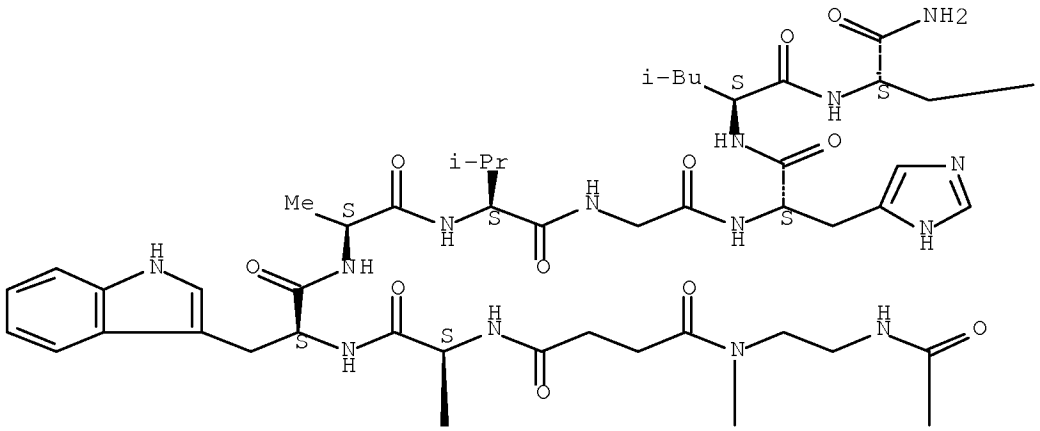
PAGE 2-B



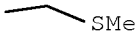
RN 808112-74-5 ZCAPLUS
CN L-Methioninamide, N2-[4-[bis[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]-1,4-dioxobutyl]-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

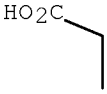
Absolute stereochemistry.

PAGE 1-A

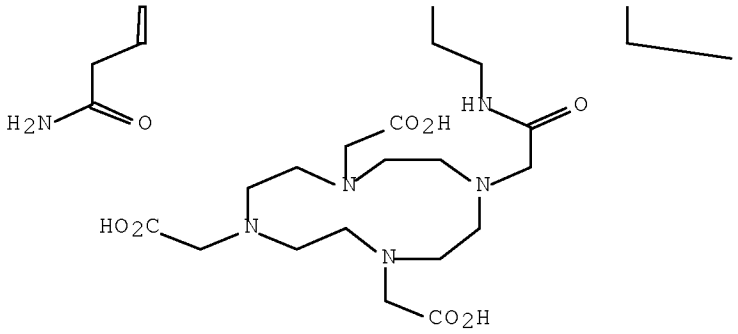


PAGE 1-B

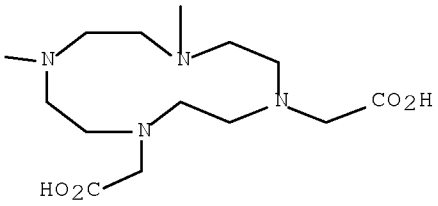




PAGE 2-A



PAGE 2-B



L80 ANSWER 19 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1355513 ZCAPLUS Full-text
DOCUMENT NUMBER: 144:99915
TITLE: Preparation of lipophilic derivatives of chelate monoamides for use in magnetic resonance imaging
INVENTOR(S): Riley, Dennis Patrick; McGhee, William D.
PATENT ASSIGNEE(S): Kereos, Inc., USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

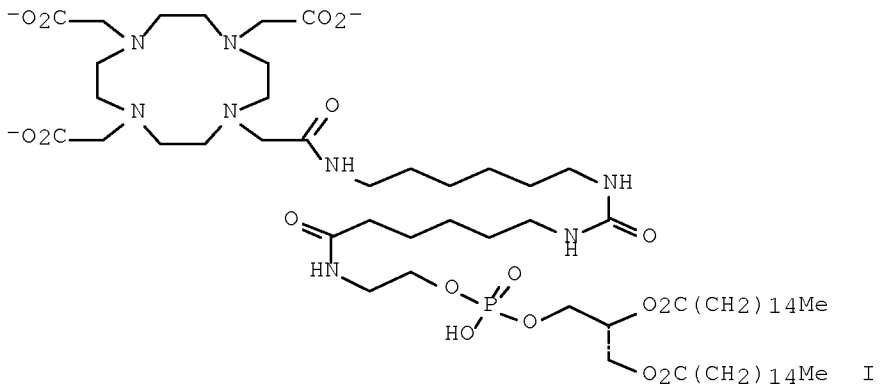
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005122891	A1	20051229	WO 2005-US19966	20050607

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,

MR, NE, SN, TD, TG
AU 2005253962 A1 20051229 AU 2005-253962 20050607
CA 2569461 A1 20051229 CA 2005-2569461 20050607
US 2006008417 A1 20060112 US 2005-146651 20050607
EP 1768558 A1 20070404 EP 2005-757440 20050607
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR
JP 2008502726 T 20080131 JP 2007-527646 20050607
PRIORITY APPLN. INFO.: US 2004-578474P P 20040609
US 2004-605180P P 20040827
WO 2005-US19966 W 20050607
OTHER SOURCE(S): CASREACT 144:99915; MARPAT 144:99915

GI



I

AB Compds. useful for associating with nanoparticle or microparticle emulsions to obtain magnetic resonance images permit control of the relaxivity of the signal and readily associate with the particulate components. The compds. are conveniently prepared from achiral derivs. of chelating moieties. Thus, the gadolinium complex of the lipophilic DOTA derivative (I) was prepared in a multistep procedure. This complex was then associated with a nanoparticle/microparticle emulsion and a targeting mol. and used in the magnetic resonance imaging of carcinoma tumors implanted in rabbits.

IC ICM A61B005-055
ICS C07D225-00

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 8

IT 7440-54-2DP, Gadolinium, DOTA monoamide derivative complexes
871560-93-9P 871560-95-1P
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of lipophilic derivs. of gadolinium-DOTA chelate monoamides for use in magnetic resonance imaging)

IT 115265-97-9P 115288-21-6P 201867-18-7P 871560-74-6P
871560-77-9P 871560-80-4P 871560-85-9P
871560-89-3P 871560-91-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of lipophilic derivs. of gadolinium-DOTA chelate monoamides for
use in magnetic resonance imaging)

IT 871560-93-9P 871560-95-1P

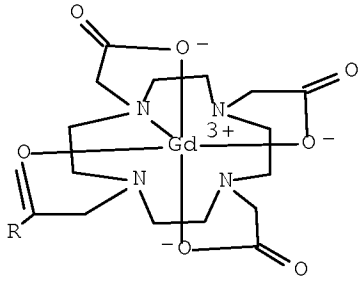
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of lipophilic derivs. of gadolinium-DOTA chelate monoamides for
use in magnetic resonance imaging)

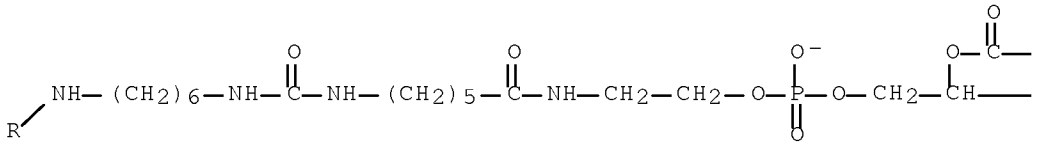
RN 871560-93-9 ZCAPLUS

CN Gadolinate(1-), [10-[23-hydroxy-23-oxido-2-(oxo-κO)-11,18,29-trioxo-26-[(1-oxohexadecyl)oxy]-22,24,28-trioxa-3,10,12,19-tetraaza-23-phosphatetratetracont-1-yl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(4-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-, hydrogen (9CI) (CA INDEX NAME)

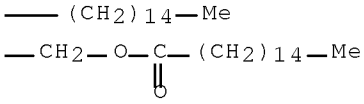
PAGE 1-A



PAGE 2-A



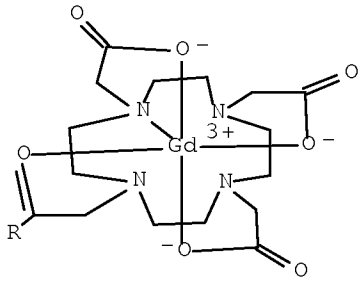
PAGE 2-B



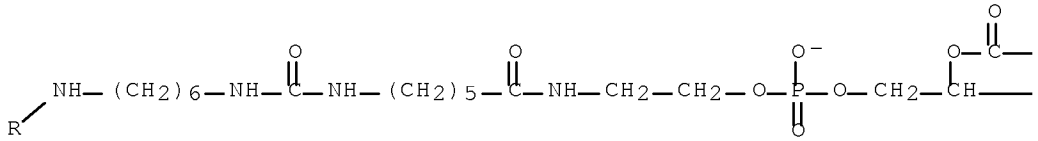
RN 871560-95-1 ZCAPLUS

CN Gadolinate(1-), [10-[23-hydroxy-23-oxido-2-(oxo-κO)-11,18,29-trioxo-26-[(1-oxohexadecyl)oxy]-22,24,28-trioxa-3,10,12,19-tetraaza-23-phosphatetratetracont-1-yl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(4-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]- (9CI) (CA INDEX NAME)

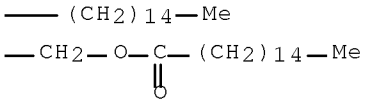
PAGE 1-A



PAGE 2-A



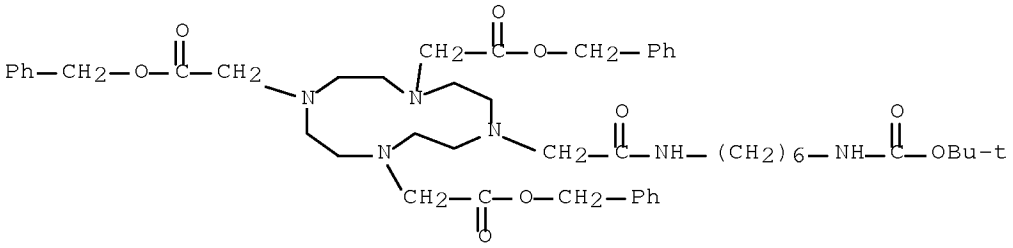
PAGE 2-B



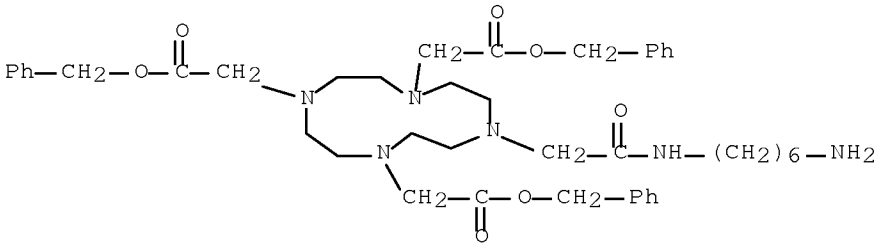
IT 871560-77-9P 871560-80-4P 871560-85-9P
871560-89-3P 871560-91-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of lipophilic derivs. of gadolinium-DOTA chelate monoamides for
use in magnetic resonance imaging)

RN 871560-77-9 ZCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[[(1,1-dimethylethoxy)carbonyl]amino]hexyl]amino]-2-oxoethyl]-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

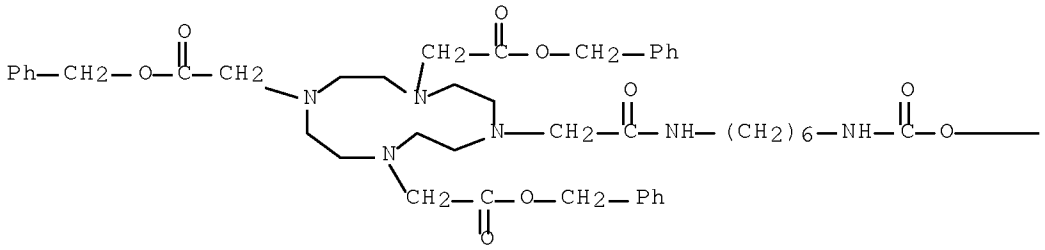


RN 871560-80-4 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-aminohexyl)amino]-2-oxoethyl]-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

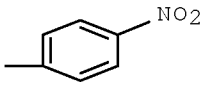


RN 871560-85-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[[(4-nitrophenoxy)carbonyl]amino]hexyl]amino]-2-oxoethyl]-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

PAGE 1-A



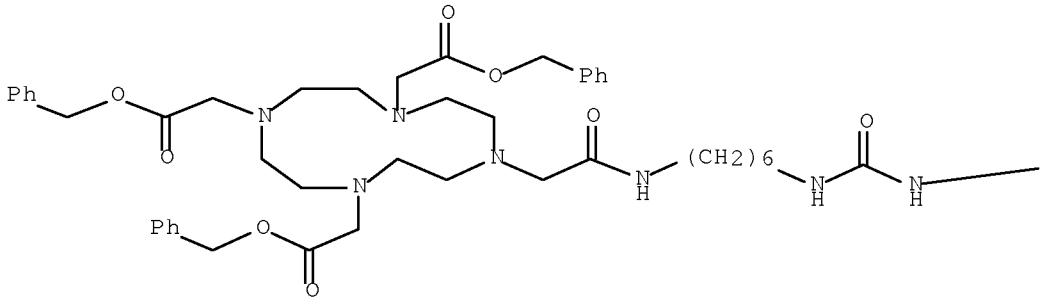
PAGE 1-B



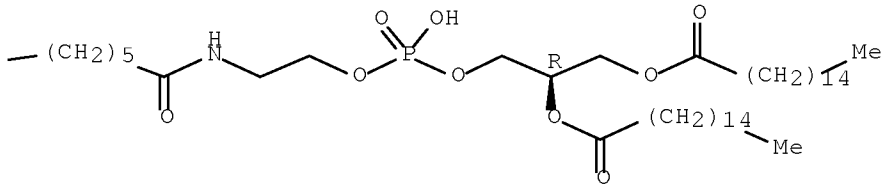
RN 871560-89-3 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[(26R)-23-hydroxy-23-oxido-2,11,18,29-tetraoxo-26-[(1-oxohexadecyl)oxy]-22,24,28-trioxa-3,10,12,19-tetraaza-23-phosphatetratetracont-1-yl]-, tris(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



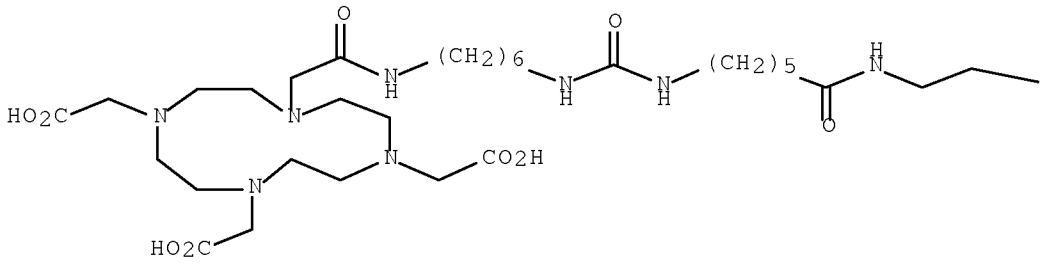
PAGE 1-B



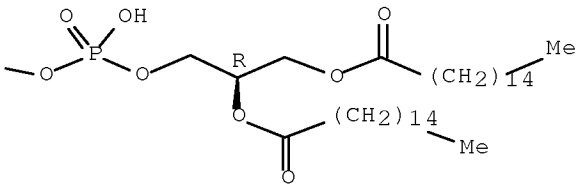
RN 871560-91-7 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[(26R)-23-hydroxy-23-oxido-2,11,18,29-tetraoxo-26-[(1-oxohexadecyl)oxy]-22,24,28-trioxa-3,10,12,19-tetraaza-23-phosphatetratetracont-1-yl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 20 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1133071 ZCAPLUS Full-text
DOCUMENT NUMBER: 144:57302
TITLE: Preparation and Characterization of a DOTA-Lysine-Biotin Conjugate as an Effector Molecule for Pretargeted Radionuclide Therapy
AUTHOR(S): Hainsworth, James; Harrison, Peter; Mather, Stephen J.
CORPORATE SOURCE: Nuclear Medicine Group, Cancer Research UK, St. Bartholomew's Hospital, London, UK
SOURCE: Bioconjugate Chemistry (2005), 16(6), 1468-1474
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pretargeted radionuclide therapy depends on the establishment of a high concentration of secondary binding sites at a tumor to which low-mol. weight radiolabeled effector mols. can be directed. This study describes the simple synthesis of an effector mol. and its subsequent characterization to determine the extent to which it complied with the ideal requirements of such a compound (ε)-DOTA-(α)-biotinamidolysine (DLB) was synthesized in high yield and purity using conventional SPPS methodol. High radiochem. purities were obtained when labeled with several potentially useful radionuclides. The radiolabeled analog bound to streptavidin efficiently with a stoichiometry similar to that of native biotin and showed high stability in serum and upon challenge with acid conditions. Biodistribution studies in normal animals showed a rapid rate of clearance from the blood and low retention of radioactivity by normal

tissues. This design of effector mol. therefore shows promise for further pretargeted radionuclide therapy studies.

CC 63-8 (Pharmaceuticals)

IT Antitumor agents
Radiotherapy
Stability
(preparation and characterization of a DOTA-lysine-biotin conjugate as an effector mol. for pretargeted radionuclide therapy)

IT 188428-79-7P 871576-45-3P 871576-46-4P 871576-47-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and characterization of a DOTA-lysine-biotin conjugate as an effector mol. for pretargeted radionuclide therapy)

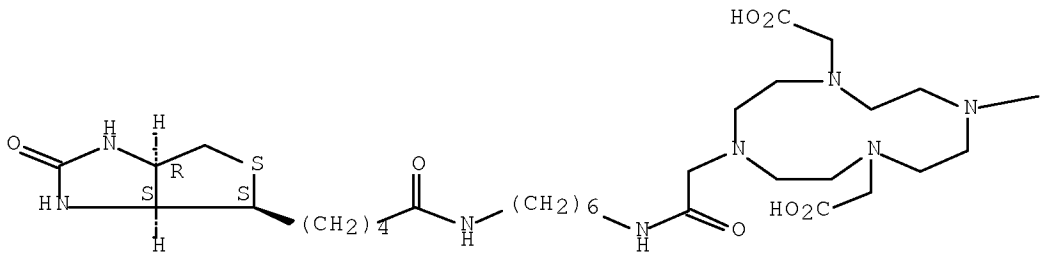
IT 871576-46-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and characterization of a DOTA-lysine-biotin conjugate as an effector mol. for pretargeted radionuclide therapy)

RN 871576-46-4 ZCAPLUS

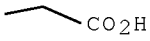
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]hexyl]amino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 21 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:673150 ZCAPLUS Full-text
DOCUMENT NUMBER: 143:168816
TITLE: Methods for imaging the lymphatic system using dendrimer-based contrast agents
INVENTOR(S): Brechbiel, Martin W.; Kobayashi, Hisataka; Choyke, Peter L.; Morris, John C.; Waldmann, Thomas A.
PATENT ASSIGNEE(S): The Government of the United States of America as

Represented by the Secretary of the Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005067982	A2	20050728	WO 2005-US1388	20050112
WO 2005067982	A3	20051027		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005171424	A1	20050804	US 2004-756948	20040113
EP 1722825	A2	20061122	EP 2005-722440	20050112
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: US 2004-756948 A 20040113
WO 2005-US1388 W 20050112

AB Methods are disclosed for lymphatic-system imaging using dendrimer conjugates as contrast agents. The disclosed methods are applicable to the imaging of all lymphatic structures, but in particular embodiments are particularly suited for imaging specific parts of the lymphatic system such as lymph nodes or lymphatic vessels. The methods permit the assessment of abnormal conditions within the lymphatic system, such as lymphoma/lymphoproliferative disease, inflammation, and cancer metastasis. The methods also may be used to identify and locate lymph nodes into which lymph fluid flows from a tumor.

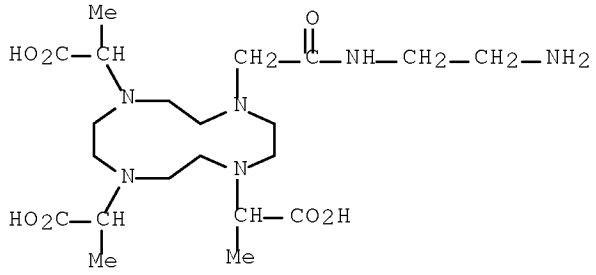
IC ICM A61K049-00
CC 8-9 (Radiation Biochemistry)

IT 67-43-6D, Dtpa, dendrimer-conjugated complexes 5109-69-3D, Doxa, dendrimer-conjugated complexes 14701-22-5D, Nickel ion (2+), dendrimer-conjugated complexes, biological studies 14913-52-1D, Neodymium ion (3+), dendrimer-conjugated complexes, biological studies 15158-11-9D, Copper ion (2+), dendrimer-conjugated complexes, biological studies 15438-31-0D, Ferrous ion, dendrimer-conjugated complexes, biological studies 16065-83-1D, Chromium ion (3+), dendrimer-conjugated complexes, biological studies 16397-91-4D, Manganese ion (2+), dendrimer-conjugated complexes, biological studies 18472-30-5D, Erbium ion (3+), dendrimer-conjugated complexes, biological studies 18923-27-8D, Ytterbium ion (3+), dendrimer-conjugated complexes, biological studies 20074-52-6D, Ferric ion, dendrimer-conjugated complexes, biological studies 22541-14-6D, Praseodymium ion (3+), dendrimer-conjugated complexes, biological studies 22541-17-9D, Samarium ion (3+), dendrimer-conjugated complexes, biological studies 22541-19-1D, Gadolinium ion (3+), dendrimer-conjugated complexes, biological studies 22541-20-4D, dendrimer-conjugated complexes, biological studies 22541-21-5D, Dysprosium ion (3+), dendrimer-conjugated complexes, biological studies 22541-22-6D, Holmium ion (3+), dendrimer-conjugated complexes, biological studies

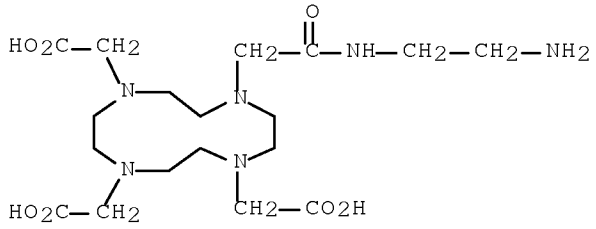
22541-53-3D, Cobalt ion (2+), dendrimer-conjugated complexes, biological studies 56491-86-2D, Nota, dendrimer-conjugated complexes 60239-18-1D, Dota, dendrimer-conjugated complexes 60239-22-7D, Teta, dendrimer-conjugated complexes 108414-96-6D, 1b4m, dendrimer-conjugated complexes 113786-33-7D, Bopta, dendrimer-conjugated complexes 114873-37-9D, DO 3A, dendrimer-conjugated complexes 120041-08-9D, Hp-do3a, dendrimer-conjugated complexes 149979-17-9D, DO 3MA, dendrimer-conjugated complexes 150467-20-2D, dendrimer-conjugated complexes 160363-61-1D, dendrimer-conjugated complexes
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(imaging the lymphatic system using dendrimer-based contrast agents)

IT 149979-17-9D, DO 3MA, dendrimer-conjugated complexes
150467-20-2D, dendrimer-conjugated complexes
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(imaging the lymphatic system using dendrimer-based contrast agents)

RN 149979-17-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-tricarboxylic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-α,α',α''-trimethyl- (9CI) (CA INDEX NAME)



RN 150467-20-2 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]- (CA INDEX NAME)



L80 ANSWER 22 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:238416 ZCAPLUS Full-text
DOCUMENT NUMBER: 142:303552
TITLE: Method and composition for the treatment of cancer by the enzymatic conversion of soluble radioactive toxic precipitates in the cancer

INVENTOR(S): Mayers, George L.; Rose, Samuel; Rose, Lottie
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 78 pp., Cont.-in-part of U.S. Ser. No. 226,288.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005058652	A1	20050317	US 2004-898585	20040723
US 2003068382	A1	20030410	US 2002-226288	20020822
PRIORITY APPLN. INFO.:			US 2002-226288	A2 20020822
			US 1999-314422	A3 19990518

AB The invention features compns. and methods for treating or alleviating a symptom of cancer. The compns. and methods of the invention direct supra-LDs of radiation, called Hot-Spots, to virtually all cancer cell types. The compns. comprise a cell-targeting agent (such as an antibody) which augments cellular uptake of the reagent linked to a platform building material by a carrier. The platform building material detaches from the targeting agent upon uptake of the reagent into the cell. Examples of such compns. are: anti-EGFR antibody-dextran-indoxylphosphate- phosphoenolpyruvate conjugate, transferrin-albumin-bis-3-indoxyl glycoside-Loracarbef conjugate, folate-Ig-porphyrin- difluoromethylornithine conjugate. Above compns. are administered with enzyme conjugates such as β-lactamase-anti-nitroiodophenol antibody, and with radiopharmaceuticals such as 131I-5-iodo-3-indoxyl galactoside.

IC ICM G01N033-53
ICS G01N033-567; A61K049-00; A61K039-395
INCL 424178100; 530391100; 435007200
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 8, 15
ST antitumor immunoconjugate immunotoxin radiopharmaceutical enzyme
IT Antitumor agents
Neoplasm
Nicotinic agonists
Peptidomimetics
Radiopharmaceuticals
Radiotherapy
(targeted immunoconjugate radiopharmaceutical compns.)
IT 59-30-3DP, Folic acid, porphyrin-Ig-difluoromethylornithine conjugate 619-66-9DP, 4-Carboxybenzaldehyde, reaction product with ornithine decarboxylase 9001-78-9DP, lactamase conjugate 9013-20-1DP, Streptavidin, UDP-N-Acetylglucosamine enolpyruvyltransferase conjugate 9023-27-2DP, UDP-N-Acetylglucosamine enolpyruvyltransferase, streptavidin conjugate 9024-60-6DP, Ornithine decarboxylase, reaction product with carboxybenzaldehyde 9031-11-2DP, lactamase conjugate 9073-60-3DP, galactosidase conjugate 10043-66-0DP, Iodine 131, compds., biological studies 10098-91-6DP, Yttrium 90, conjugated complexes, biological studies 37293-51-9DP, Aminodextran, antibody conjugate 40704-75-4DP, N-(2-Hydroxypropyl)methacrylamide polymer, crosslinked conjugates 61449-63-6DP, folate-Ig-difluoromethylornithine conjugate 62229-50-9DP, Egf, Loracarbef-polymer conjugates 70052-12-9DP, porphyrin-Ig-folate conjugate 76470-66-1DP, Loracarbef, conjugates 847944-58-5DP, antibody-dextran conjugate 847944-59-6DP, antibody-dextran conjugate 847944-60-9DP, antibody-dextran conjugate 847944-61-0DP, albumin-transferrin conjugate 847944-62-1P 847944-64-3DP, EGF-Loracarbef conjugates 847944-66-5DP, yttrium 90 complexes 847944-67-6P 847944-68-7P 847944-69-8P 847944-70-1P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(targeted immunoconjugate radiopharmaceutical compns.)

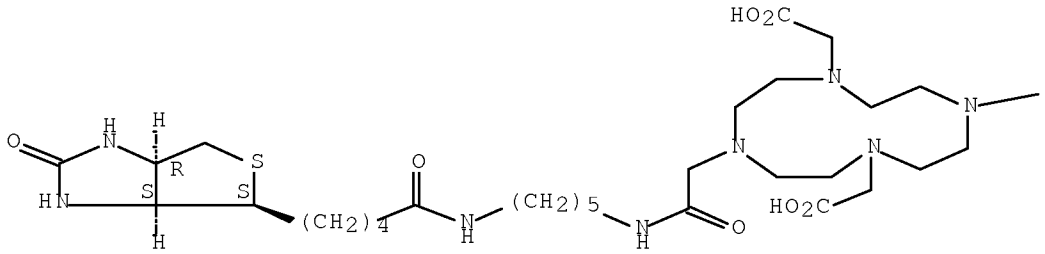
IT 847944-66-5DP, yttrium 90 complexes
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(targeted immunoconjugate radiopharmaceutical compns.)

RN 847944-66-5 ZCAPLUS

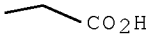
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[5-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]pentyl]amino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L80 ANSWER 23 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:14435 ZCAPLUS Full-text

DOCUMENT NUMBER: 142:107822

TITLE: Pharmaceutical composition comprising somatostatin analog

INVENTOR(S): Lambert, Oliver; Moser, Katrin

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

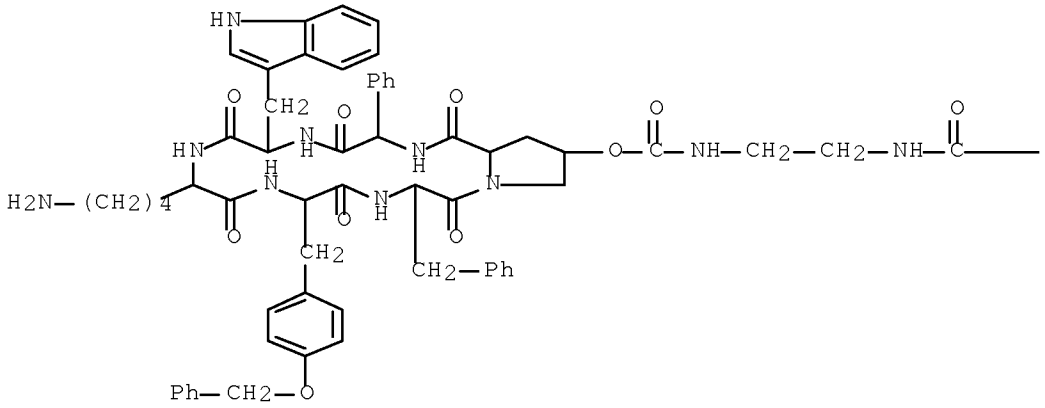
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000893	A2	20050106	WO 2004-EP6794	20040623
WO 2005000893	A3	20050407		

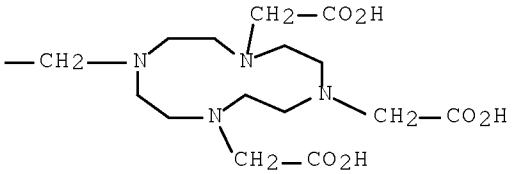
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,

```
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
            AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
            EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
            SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
            SN, TD, TG
     AU 2004251866        A1    20050106    AU 2004-251866         20040623
     CA 2529449           A1    20050106    CA 2004-2529449        20040623
     EP 1648934           A2    20060426    EP 2004-740213         20040623
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
     CN 1812997           A     20060802    CN 2004-80017884       20040623
     BR 2004011820        A     20060808    BR 2004-11820          20040623
     JP 2007536195        T     20071213    JP 2006-516037         20040623
     US 2007093412        A1    20070426    US 2005-560751         20051214
     MX 2005PA13821       A     20060228    MX 2005-PA13821        20051216
     NO 2006000375        A     20060124    NO 2006-375            20060124
PRIORITY APPLN. INFO.:                       GB 2003-14695       A  20030624
                                             GB 2003-25388       A  20031030
                                             WO 2004-EP6794      W  20040623
OTHER SOURCE(S):         MARPAT 142:107822
AB    The present invention describes parenteral pharmaceutical compns. comprising a
      somatostatin analog and novel somatostatin analogs.
IC    ICM  C07K014-655
      ICS  A61K038-31; C07K007-06
CC    2-5 (Mammalian Hormones)
      Section cross-reference(s): 34, 63
IT    Antitumor agents
      Cushing's syndrome
      Drug delivery systems
      Neoplasm
         (pharmaceutical composition comprising somatostatin analog)
IT    820232-46-0P   820232-47-1P 820232-48-2P
      RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
      (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
      (Uses)
         (pharmaceutical composition comprising somatostatin analog)
IT    820232-48-2P
      RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
      (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
      (Uses)
         (pharmaceutical composition comprising somatostatin analog)
RN    820232-48-2  ZCAPLUS
CN    Cyclo[(2R)-2-phenylglycyl-D-tryptophyl-L-lysyl-O-(phenylmethyl)-L-tyrosyl-
      L-phenylalanyl-(4R)-4-[[[[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-
      tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]carbonyl]oxy]-L-prolyl]
      (9CI)  (CA INDEX NAME)
```

PAGE 1-A



PAGE 1-B



L80 ANSWER 24 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:657986 ZCAPLUS Full-text
DOCUMENT NUMBER: 137:190759
TITLE: Amino derivatives of biotin and their conjugates with macrocyclic chelating agents
INVENTOR(S): Paganelli, Giovanni; Chinol, Marco; Ginanneschi, Mauro
PATENT ASSIGNEE(S): Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Italy
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066075	A2	20020829	WO 2002-IT91	20020215
WO 2002066075	A3	20030130		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2436242	A1	20020829	CA 2002-2436242		20020215
AU 2002237517	A1	20020904	AU 2002-237517		20020215
EP 1359943	A2	20031112	EP 2002-703851		20020215
EP 1359943	B1	20051012			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
HU 2003003151	A2	20031229	HU 2003-3151		20020215
BR 2002007327	A	20040210	BR 2002-7327		20020215
JP 2004524305	T	20040812	JP 2002-565633		20020215
CN 1531445	A	20040922	CN 2002-805086		20020215
AT 306283	T	20051015	AT 2002-703851		20020215
ES 2248522	T3	20060316	ES 2002-703851		20020215
MX 2003PA07317	A	20040630	MX 2003-PA7317		20030815
US 2004067199	A1	20040408	US 2003-468075		20030930
PRIORITY APPLN. INFO.:			IT 2001-RM79	A	20010216
			WO 2002-IT91	W	20020215

OTHER SOURCE(S): MARPAT 137:190759

AB Amino biotin derivs. are prepared and used for the preparation of conjugates with radionuclides for use in human and animal therapy and diagnostics, particularly for the diagnosis and therapy of pathol. conditions such as tumors. A reduced biotinylhexamethylenediamine conjugate with DOTA was prepared

IC ICM A61K051-04

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 8, 26

IT Antitumor agents
Chelating agents
Diagnostic agents
Radiopharmaceuticals
Radiotherapy
(amino derivs. of biotin and their conjugates with macrocyclic chelating agents)

IT 451478-45-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino derivs. of biotin and their conjugates with macrocyclic chelating agents)

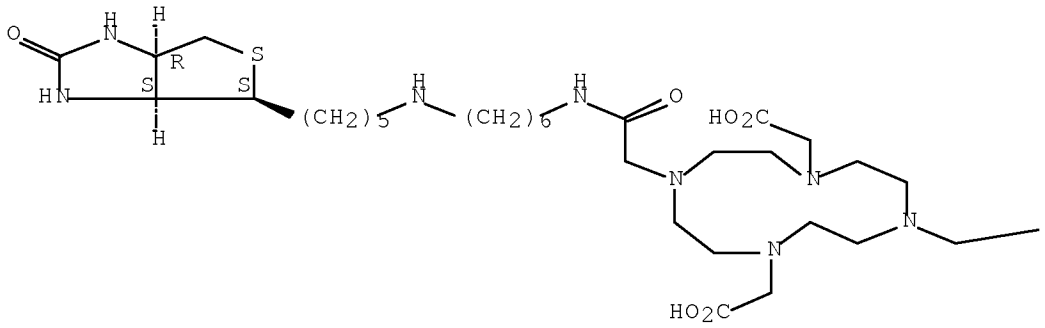
IT 451478-45-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino derivs. of biotin and their conjugates with macrocyclic chelating agents)

RN 451478-45-8 ZCAPLUS

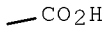
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]pentyl]amino]hexyl]amino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L80 ANSWER 25 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:107368 ZCAPLUS Full-text
DOCUMENT NUMBER: 136:167700
TITLE: Preparation of somatostatin analogues for pharmaceutical use
INVENTOR(S): Albert, Rainer; Bauer, Wilfried; Bodmer, David; Bruns, Christian; Felner, Ivo; Hellstern, Heribert; Lewis, Ian; Meisenbach, Mark; Weckbecker, Gisbert; Wietfeld, Bernhard
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.; et al.
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010192	A2	20020207	WO 2001-EP8824	20010730
WO 2002010192	A3	20020919		
WO 2002010192	A9	20021017		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

TW 282341	B	20070611	TW 2001-90118314		20010726
CA 2416293	A1	20020207	CA 2001-2416293		20010730
EP 1307486	A2	20030507	EP 2001-969555		20010730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001012859	A	20030701	BR 2001-12859		20010730
HU 2003000684	A2	20030929	HU 2003-684		20010730
HU 2003000684	A3	20040830			
JP 2004505095	T	20040219	JP 2002-515921		20010730
JP 3829118	B2	20061004			
NZ 523836	A	20040827	NZ 2001-523836		20010730
RU 2287533	C2	20061120	RU 2003-105817		20010730
ZA 2003000406	A	20040402	ZA 2003-406		20030115
IN 2003CN00143	A	20050408	IN 2003-CN143		20030123
NO 2003000484	A	20030319	NO 2003-484		20030130
MX 2003PA00991	A	20030609	MX 2003-PA991		20030131
US 2005014686	A1	20050120	US 2003-343288		20030826
PRIORITY APPLN. INFO.:			GB 2000-18891	A	20000801
			WO 2001-EP8824	W	20010730

AB The invention provides cyclo[{4-(NH2-C2H4-NH-CO-O-)Pro}-Phg-DTrp-Lys-Tyr(4-Benzyl)-Phe] (I) , optionally in protected form, or a pharmaceutically acceptable salt or complex thereof, which has interesting pharmaceutical properties. The ability of I to bind to human somatostatin receptors, inhibit GH release, and decrease IGF-1 plasma levels is exemplified. Pharmaceutical compns. containing the analogs are also claimed.

IC ICM C07K007-00

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 2

IT Antitumor agents
(pancreas; preparation of somatostatin analogs for pharmaceutical use)

IT Angiogenesis inhibitors
Antidiarrheals
Antitumor agents
Diagnosis
Drug delivery systems
Human
(preparation of somatostatin analogs for pharmaceutical use)

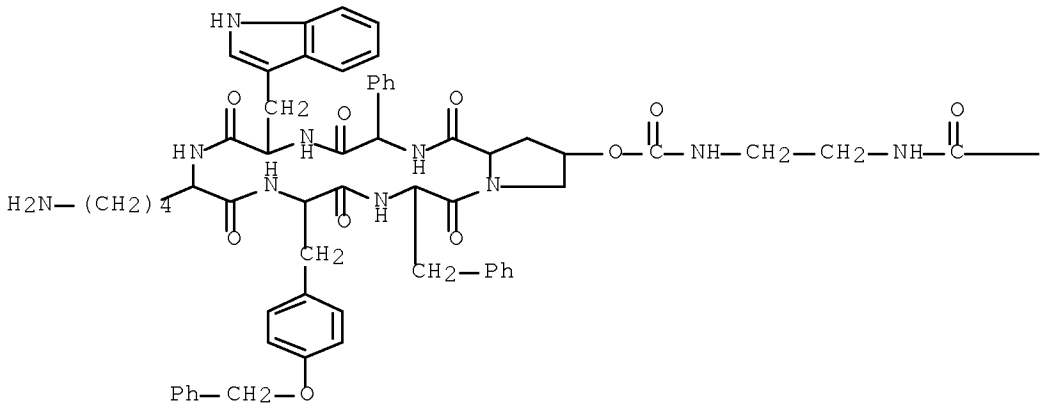
IT 396091-82-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of somatostatin analogs for pharmaceutical use in combination with other drugs)

IT 396091-82-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of somatostatin analogs for pharmaceutical use in combination with other drugs)

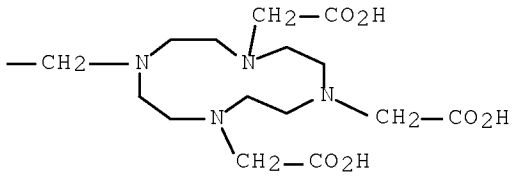
RN 396091-82-0 ZCAPLUS

CN Cyclo[(2S)-2-phenylglycyl-D-tryptophyl-L-lysyl-O-(phenylmethyl)-L-tyrosyl-L-phenylalanyl-(4R)-4-[[[[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]carbonyl]oxy]-L-prolyl] (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L80 ANSWER 26 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:935597 ZCAPLUS Full-text
DOCUMENT NUMBER: 136:54028
TITLE: Preparation of vitronectin receptor antagonist pharmaceuticals
INVENTOR(S): Rajopadhye, Milind; Barrett, John A.; Carpenter, Alan P., Jr.; Cheesman, Edward H.; Harris, Thomas D.
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 449 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001098294	A2	20011227	WO 2001-US19794	20010621
WO 2001098294	A3	20030109		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2413957	A1	20011227	CA 2001-2413957	20010621
AU 2001070025	A5	20020102	AU 2001-70025	20010621
EP 1296678	A2	20030402	EP 2001-948554	20010621

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:	US 2000-213212P	P 20000621
	WO 2001-US19794	W 20010621

OTHER SOURCE(S): MARPAT 136:54028

AB Compds. (Q)d-Ln-(Ch)d' (Q is a residue having an indazole-type moiety , d = 1-10, d' = 1-100, Ln is a linking group, Ch is a metal-bonding unit) were prepared for use in the diagnosis and treatment of cancer. The present invention provides novel compds. useful for the treatment of rheumatoid arthritis. Thus, 2-[[[4-[4-[[[3-[2-[2-[3-[[6-[[1-aza-2-(2-sulfophenyl)vinyl]amino](3-pyridyl)]carbonylamino]propoxy]ethoxy]ethoxy]propyl]amino]sulfonyl]phenyl]phenyl]sulfonyl]amino]-3-[[1-[3-(indazole-2-ylamino)propyl](1H-indazol-5-yl)]carbonylamino]propanoic acid was prepared (claimed compound). Syntheses of radiopharmaceticals, e.g., 99mTc(VnA)(tricine)(phosphine), where VnA represents the vitronectin receptor antagonist, are also described.

IC ICM C07D403-00

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 8, 28, 63, 78

IT Angiogenesis
Antitumor agents
Atherosclerosis
Radiopharmaceuticals
Rheumatoid arthritis
(preparation of vitronectin receptor antagonist pharmaceuticals)

IT 5704-04-1DP, Tricine, amino acid derivative, TPPTS technetium-99m complexes
277328-73-1P 277328-74-2P 277328-75-3P 277328-76-4P 277328-78-6P
277328-79-7P 277328-80-0P 277328-81-1P 277328-82-2P 277328-83-3P
277328-84-4P 277328-85-5P 277328-86-6P 277328-87-7P 277328-88-8P
277328-89-9P 277328-90-2P 277328-91-3P 277328-92-4P 277328-93-5P
277328-94-6P 277328-95-7P 277328-96-8P 277328-97-9P 277328-98-0P
277328-99-1P 277329-00-7P 277329-01-8P 277329-02-9P
277329-03-0P 277329-04-1P 277329-05-2P 277329-06-3P
277329-07-4P 277329-08-5P 277329-09-6DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 277329-10-9DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 277329-11-0DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 277329-12-1DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 277329-13-2DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 277329-14-3DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 277332-11-3DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 278174-58-6P
278174-59-7P 278174-60-0P 278174-61-1P 278174-62-2P 278174-63-3P
278174-64-4P 278174-65-5P 278174-66-6P 278174-67-7P 278174-68-8P
278174-69-9P 278174-70-2P 278174-71-3P 278177-22-3DP, indium-111-labeled 278177-32-5DP, yttrium-90-labeled
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

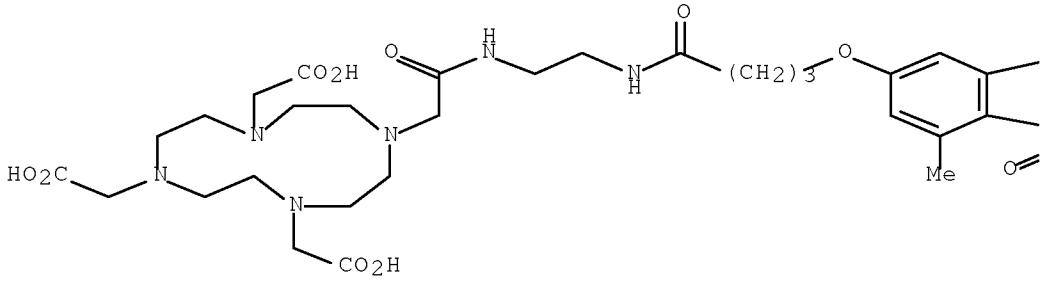
(Uses)
(preparation of vitronectin receptor antagonist pharmaceuticals)

IT 277329-03-0P 277329-06-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of vitronectin receptor antagonist pharmaceuticals)

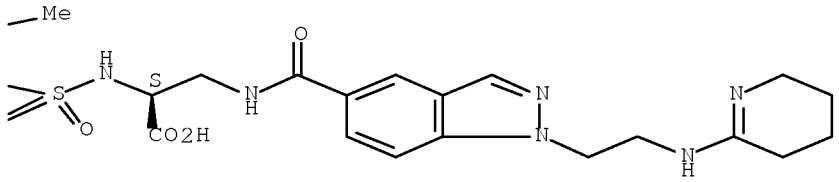
RN 277329-03-0 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[4-[4-[[[(1S)-1-carboxy-2-[[[1-[2-[(3,4,5,6-tetrahydro-2-pyridinyl)amino]ethyl]-1H-indazol-5-yl]carbonyl]amino]ethyl]amino]sulfonyl]-3,5-dimethylphenoxy]-1-oxobutyl]amino]ethyl]amino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



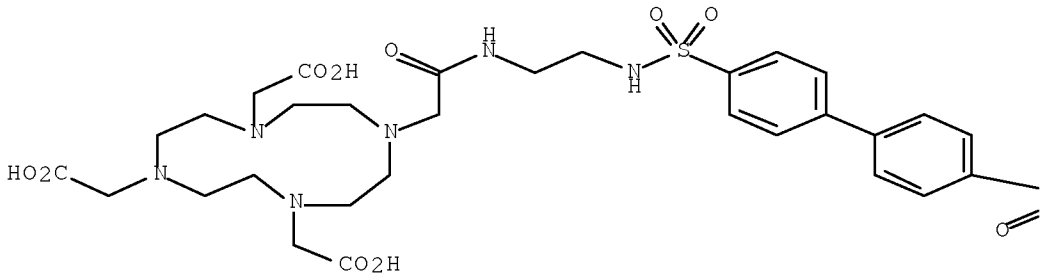
PAGE 1-B



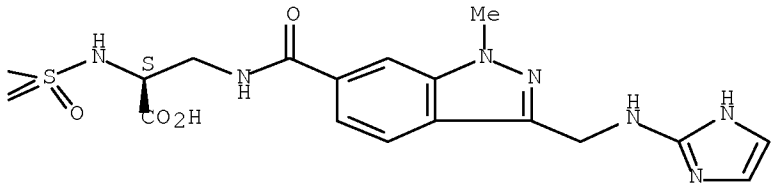
RN 277329-06-3 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[[4'-[[[(1S)-1-carboxy-2-[[[3-[(1H-imidazol-2-ylamino)methyl]-1-methyl-1H-indazol-6-yl]carbonyl]amino]ethyl]amino]sulfonyl][1,1'-biphenyl]-4-yl]sulfonyl]amino]ethyl]amino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L80 ANSWER 27 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:420991 ZCAPLUS Full-text
DOCUMENT NUMBER: 133:59098
TITLE: Preparation of vitronectin receptor antagonist pharmaceuticals
INVENTOR(S): Rajopadhye, Milind; Harris, Thomas David; Cheesman, Edward H.
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 362 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035488	A2	20000622	WO 1999-US30312	19991217
WO 2000035488	A3	20001109		
W: AL, AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6322770	B1	20011127	US 1999-281207	19990330
US 2002015680	A1	20020207	US 1999-281209	19990330

US 6524553	B2	20030225			
US 6548663	B1	20030415	US 1999-281050		19990330
CA 2346935	A1	20000622	CA 1999-2346935		19991217
AU 2000023715	A	20000703	AU 2000-23715		19991217
EP 1140203	A2	20011010	EP 1999-967442		19991217
EP 1140203	B1	20070523			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY					
TR 200101775	T2	20020722	TR 2001-1775		19991217
AT 362772	T	20070615	AT 1999-967442		19991217
ES 2288040	T3	20071216	ES 1999-967442		19991217
US 2003124120	A1	20030703	US 2002-269252		20021011
US 2003149262	A1	20030807	US 2002-306054		20021126
PRIORITY APPLN. INFO.:			US 1998-112829P	P	19981218
			US 1998-80150P	P	19980331
			US 1998-112715P	P	19981218
			US 1998-112732P	P	19981218
			US 1998-112831P	P	19981218
			US 1999-281050	A3	19990330
			US 1999-281209	A3	19990330
			WO 1999-US30312	W	19991217

OTHER SOURCE(S): MARPAT 133:59098

AB Compds. (Q)d-Ln-Ch (Q is a residue having an indazole-type moiety , d = 1-10, Ln is a linking group, Ch is a metal-bonding unit) were prepared for use in the diagnosis and treatment of cancer, methods of imaging tumors in a patient, and methods of treating cancer in a patient. The present invention also provides novel compds. useful for monitoring therapeutic angiogenesis treatment and destruction of new angiogenic vasculature. Thus, 2-[[[4-[4-[[[3-[2-[2-[3-[[6-[[1-aza-2-(2-sulfophenyl)vinyl]amino](3-pyridyl)]carbonylamino]propoxy]ethoxy]ethoxy]propyl]amino]sulfonyl]phenyl]phenyl]sulfonyl]amino]-3-[[1-[3-(indazole-2-ylamino)propyl](1H-indazol-5-yl)]carbonylamino]propanoic acid was prepared (claimed compound). Syntheses of radiopharmaceuticals, e.g., 99mTc(VnA)(tricine)(phosphine), where VnA represents the vitronectin receptor antagonist, are also described.

IC ICM A61K047-48
ICS A61K049-00; A61K051-04

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 8, 28, 63, 78

IT Angiogenesis
Antitumor agents
Atherosclerosis
Radiopharmaceuticals
Rheumatoid arthritis
(preparation of vitronectin receptor antagonist pharmaceuticals)

IT 5704-04-1DP, Tricine, amino acid derivative, TPPTS technetium-99m complexes 14133-76-7DP, Technetium-99, amino acid derivative, tricine and TPPTS complexes, preparation 63995-70-0DP, TPPTS, amino acid derivative, tricine technetium-99m complexes 277328-73-1P 277328-74-2P 277328-75-3P 277328-76-4P 277328-78-6P 277328-79-7P 277328-80-0P 277328-81-1P 277328-82-2P 277328-83-3P 277328-84-4P 277328-85-5P 277328-86-6P 277328-87-7P 277328-88-8P 277328-89-9P 277328-90-2P 277328-91-3P 277328-92-4P 277328-93-5P 277328-94-6P 277328-95-7P 277328-96-8P 277328-97-9P 277328-98-0P 277328-99-1P 277329-00-7P 277329-01-8P 277329-02-9P 277329-03-0P 277329-04-1P 277329-05-2P 277329-06-3P 277329-07-4P 277329-08-5P 277329-09-6DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 277329-10-9DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 277329-11-0DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 277329-12-1DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 277329-13-2DP, technetium-99m,

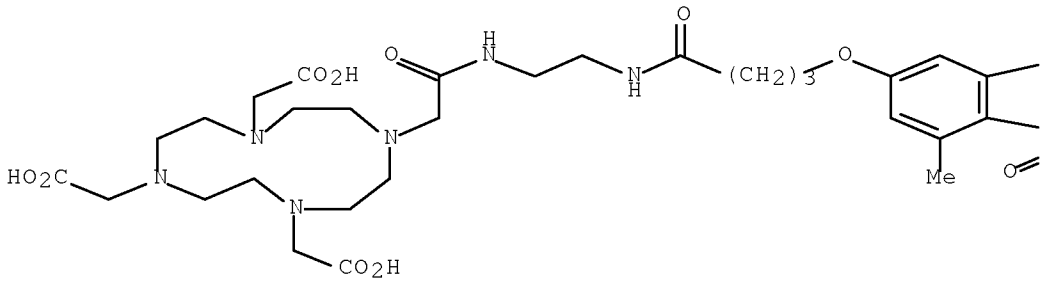
tricine tris(m-sulfophenyl)-phosphine complexes 277329-14-3DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 277332-11-3DP, technetium-99m, tricine tris(m-sulfophenyl)-phosphine complexes 278174-58-6P 278174-59-7P 278174-60-0P 278174-61-1P 278174-62-2P 278174-63-3P 278174-64-4P 278174-65-5P 278174-66-6P 278174-67-7P 278174-68-8P 278174-69-9P 278174-70-2P 278174-71-3P 278177-22-3DP, indium-111-labeled 278177-32-5DP, yttrium-90-labeled
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of vitronectin receptor antagonist pharmaceuticals)

IT 277329-03-0P 277329-06-3P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of vitronectin receptor antagonist pharmaceuticals)

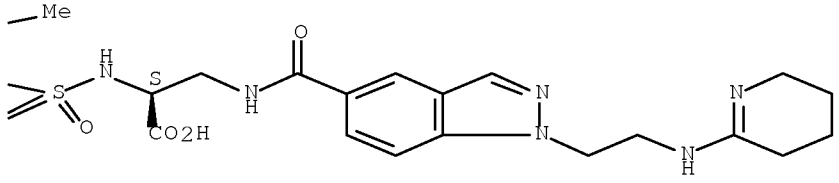
RN 277329-03-0 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[4-[4-[[[(1S)-1-carboxy-2-[[[1-[2-[(3,4,5,6-tetrahydro-2-pyridinyl)amino]ethyl]-1H-indazol-5-yl]carbonyl]amino]ethyl]amino]sulfonyl]-3,5-dimethylphenoxy]-1-oxobutyl]amino]ethyl]amino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



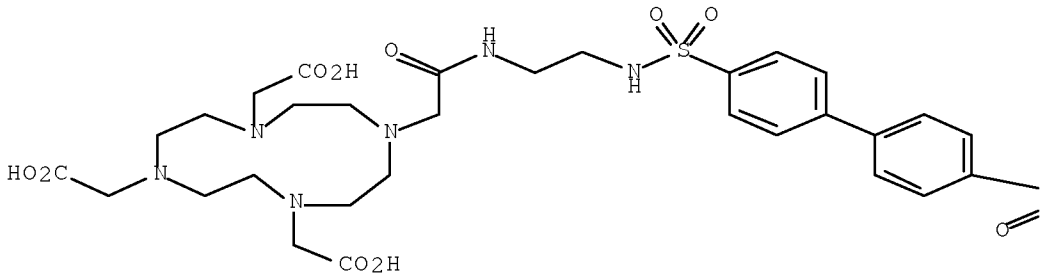
PAGE 1-B



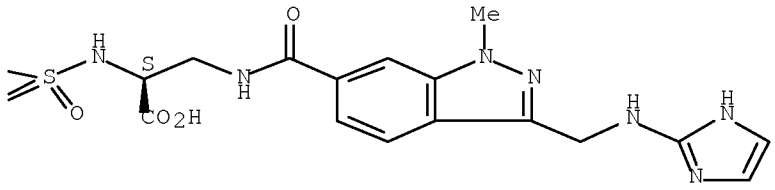
RN 277329-06-3 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[[4'-[[[(1S)-1-carboxy-2-[[[3-[(1H-imidazol-2-ylamino)methyl]-1-methyl-1H-indazol-6-yl]carbonyl]amino]ethyl]amino]sulfonyl][1,1'-biphenyl]-4-yl]sulfonyl]amino]ethyl]amino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L80 ANSWER 28 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:64531 ZCAPLUS Full-text
DOCUMENT NUMBER: 133:39944
TITLE: Synthesis, characterization, and imaging performance of a new class of macrocyclic hepatobiliary MR contrast agents
AUTHOR(S): Marinelli, Edmund R.; Neubeck, Richard; Song, Bo; Wagler, Thomas; Ranganathan, Ramachandran S.; Sukumaran, Kozikhott; Wedeking, Paul W.; Nunn, Adrian; Runge, Val M.; Tweedle, Michael F.
CORPORATE SOURCE: Bracco Research USA, Princeton, NJ, 08540, USA
SOURCE: Investigative Radiology (2000), 35(1), 8-24
CODEN: INVRAV; ISSN: 0020-9996
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB RATIONALE AND OBJECTIVES. To investigate the effect of substituent lipophilicity, substituent position, and overall charge on the hepatobiliary clearance and tolerance of a series of aromatic ring-containing macrocyclic Gd chelates to select a candidate compound for evaluation as a hepatobiliary imaging agent. METHODS. Hepatobiliary clearance was studied in rats. Tissue distribution and tolerance were studied in mice. Imaging was performed in cats, rabbits, and Rhesus monkeys using T1-weighted pulse sequences or T1-weighted breath-hold pulse sequences. RESULTS. All the compds. were excreted bimodally. Gd-2,5-BPA-DO3A was found to have the optimal combination of hepatobiliary clearance (47% in rats, 29% in mice) and tolerance (min. LD 5.0

mmol/kg). Initial imaging studies in cats demonstrated the feasibility of Gd-2,5-BPA-DO3A for hepatic imaging. In rabbits with implanted VX-2 adenocarcinoma as a model for metastatic liver disease, Gd-2,5-BPA-DO3A provided sustained hepatic signal intensity (SI) enhancement and lesion conspicuity over a 120-min imaging time course. In Rhesus monkeys with normal liver function, Gd-2,5-BPA-DO3A afforded sustained hepatic SI enhancement and a time-dependent increase in gallbladder SI over the entire 90-min imaging time course. CONCLUSIONS. Gd-2,5-BPA-DO3A provides dramatic and sustained SI enhancement of hepatic tissue in cats, rabbits, and Rhesus monkeys that was superior in all respects to the extracellular space MRI agent, Gd-HP-DO3A, that was employed as a control.

CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 78

IT Imaging
(tumor; synthesis, characterization, and imaging performance of macrocyclic Gd chelates as hepatobiliary MR contrast agents)

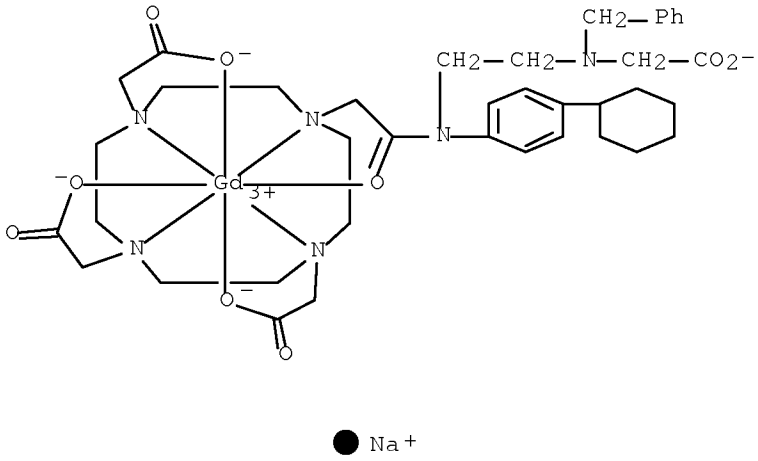
IT 7440-54-2DP, Gadolinium, complexes, biological studies 173526-55-1P 173526-57-3P 173526-61-9P 173526-65-3P 173526-70-0P 173526-77-7P 173526-81-3P 275801-54-2P 275801-55-3P 275801-56-4P 275801-57-5P
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(synthesis, characterization, and imaging performance of macrocyclic Gd chelates as hepatobiliary MR contrast agents)

IT 84827-47-4P 167867-06-3P 173526-69-7P 173526-80-2P 173526-83-5P 173526-84-6P 173526-85-7P 173526-86-8P 173526-88-0P 173526-89-1P 173526-90-4P 173526-91-5P 173526-93-7P 173526-94-8P 173527-03-2P 173527-04-3P 173527-05-4P 173527-12-3P 173527-13-4P 173527-14-5P 173527-20-3P 173527-21-4P 173527-22-5P 275371-48-7P 275371-49-8P 275371-50-1P 275371-51-2P 275371-52-3P 275371-53-4P 275371-54-5P 275371-55-6P 275371-56-7P 275371-59-0P 275371-60-3P 275371-61-4P 275371-62-5P 275371-63-6P 275371-64-7P 275371-65-8P 275371-67-0P 275371-68-1P 275371-70-5P 275371-72-7P 275371-73-8P 275371-74-9P 275371-75-0P 275371-77-2P 275371-78-3P 275371-80-7P 275371-81-8P 275371-85-2P 275371-87-4P 275371-90-9P 275371-91-0P 275371-92-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, characterization, and imaging performance of macrocyclic Gd chelates as hepatobiliary MR contrast agents)

IT 275801-57-5P
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(synthesis, characterization, and imaging performance of macrocyclic Gd chelates as hepatobiliary MR contrast agents)

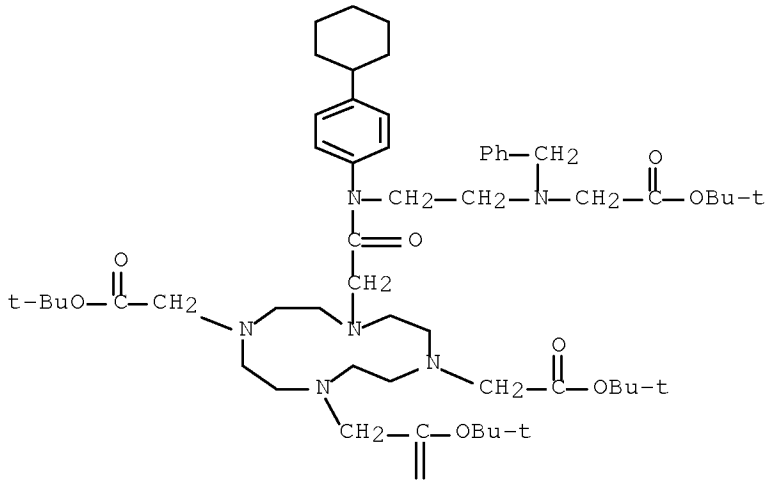
RN 275801-57-5 ZCAPLUS

CN Gadolinate(1-), [10-[2-[[2-[(carboxymethyl)(phenylmethyl)amino]ethyl](4-cyclohexylphenyl)amino]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(4-)-κN1,κN4,κN7,.kappa.N10,κO1,κO4,κO7]-, sodium (9CI) (CA INDEX NAME)



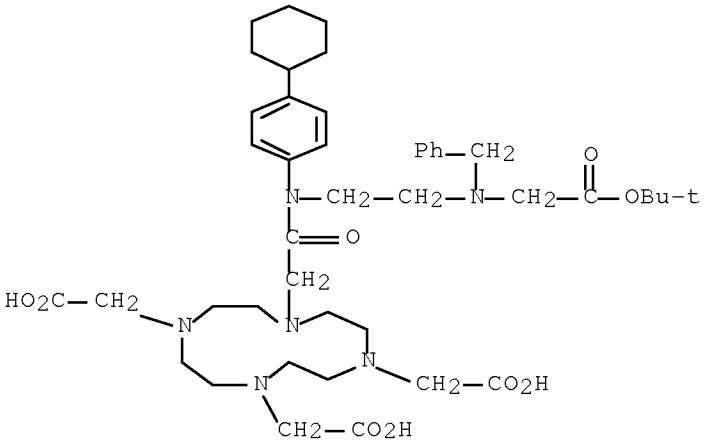
IT 173527-05-4P 275371-67-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis, characterization, and imaging performance of macrocyclic Gd chelates as hepatobiliary MR contrast agents)
RN 173527-05-4 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(4-cyclohexylphenyl)[2-[[2-(1,1-dimethylethoxy)-2-oxoethyl](phenylmethyl)amino]ethyl]amino]-2-oxoethyl]-, tris(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

RN 275371-67-0 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(4-cyclohexylphenyl)[2-[[2-(1,1-dimethylethoxy)-2-oxoethyl](phenylmethyl)amino]ethyl]amino]-2-oxoethyl]- (CA INDEX NAME)



REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L80 ANSWER 29 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:401701 ZCAPLUS Full-text
DOCUMENT NUMBER: 131:55892
TITLE: DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol
INVENTOR(S): Griffiths, Gary L.; Hansen, Hans; Govindan, Serengulam V.
PATENT ASSIGNEE(S): Immunomedics, Inc., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 19
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930745	A2	19990624	WO 1998-US26579	19981215
WO 9930745	A3	20000113		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6120768	A	20000919	US 1997-990843	19971215

AU 9918258 A 19990705 AU 1999-18258 19981215
PRIORITY APPLN. INFO.: US 1997-990843 A1 19971215
US 1993-62662 B1 19930517
US 1995-409960 A2 19950323
US 1995-486166 B2 19950607
US 1996-688781 A2 19960731
WO 1998-US26579 W 19981215
OTHER SOURCE(S): MARPAT 131:55892

AB A radionuclide-chelator conjugate composition for detecting and/or treating lesions in a patient in a pre-targeting protocol comprises pre-targeting the target cell, tissue, or pathogen with a substrate, using a targeting protein that specifically binds a marker substance on the target cell, tissue, or pathogen and to which the substrate is directly or indirectly bound; parenterally injecting the detection or therapeutic composition of the invention which comprises a chelate conjugate of biotin, a chelator, and a chelatable detection or therapeutic agent, and allowing the composition to accrete at the targeted cell, tissue, or pathogen; wherein the chelate conjugate is purified by chromatog. after chelate formation, or further comprises a blood transit-modifying linker or addend that is covalently bound within the chelate conjugate, or both; and using the detection or therapeutic agent to detect or treat the targeted cell, tissue, or pathogen.

IC ICM A61K051-00
CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 28, 63, 78
IT Anti-infective agents
Antimicrobial agents
Antitumor agents
Cardiovascular agents
Diagnosis
Drug targeting
Infection
Neoplasm
Paramagnetic materials
Parasiticides
(DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)
IT Antitumor agents
(carcinoma; DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)
IT Antitumor agents
(glioma; DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)
IT Antitumor agents
(leukemia; DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)
IT Antitumor agents
(lymphoma; DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)
IT Antitumor agents
(melanoma; DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)
IT Antitumor agents
(myeloma; DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)
IT Antitumor agents
(neuroblastoma; DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)
IT Antitumor agents
(sarcoma; DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)

IT 153-94-6D, D-Tryptophan, linker between biotin and DOTA 319-78-8D, D-Isoleucine, linker between biotin and DOTA 328-38-1D, D-Leucine, linker between biotin and DOTA 556-02-5D, D-Tyrosine, linker between biotin and DOTA 640-68-6D, D-Valine, linker between biotin and DOTA 673-06-3D, D-Phenylalanine, linker between biotin and DOTA 923-27-3D, D-Lysine, linker between biotin and DOTA 10043-49-9D, Gold-198, complexes with biotin-linked-DOTA conjugates, biological studies 10098-91-6D, Yttrium-90, complexes with biotin-linked-DOTA conjugates, biological studies 13967-65-2D, Holmium-166, complexes with biotin-linked-DOTA conjugates, biological studies 13968-53-1D, Ruthenium-103, complexes with biotin-linked-DOTA conjugates, biological studies 13981-51-6D, Mercury-197, complexes with biotin-linked-DOTA conjugates, biological studies 14119-09-6D, Gallium-67, complexes with biotin-linked-DOTA conjugates, biological studies 14119-24-5D, Osmium-191, complexes with biotin-linked-DOTA conjugates, biological studies 14133-76-7D, Technetium-99, complexes with biotin-linked-DOTA conjugates, biological studies 14191-64-1D, Praseodymium-142, complexes with biotin-linked-DOTA conjugates, biological studies 14265-75-9D, Lutetium-177, complexes with biotin-linked-DOTA conjugates, biological studies 14265-85-1D, Actinium-225, complexes with biotin-linked-DOTA conjugates, biological studies 14331-95-4D, Ruthenium-105, complexes with biotin-linked-DOTA conjugates, biological studies 14378-26-8D, Rhenium-188, complexes with biotin-linked-DOTA conjugates, biological studies 14391-11-8D, Gold-199, complexes with biotin-linked-DOTA conjugates, biological studies 14391-19-6D, Terbium-161, complexes with biotin-linked-DOTA conjugates, biological studies 14391-96-9D, Scandium-47, complexes with biotin-linked-DOTA conjugates, biological studies 14687-25-3D, Lead-203, complexes with biotin-linked-DOTA conjugates, biological studies 14885-78-0D, Indium-113, complexes with biotin-linked-DOTA conjugates, biological studies 14913-49-6D, Bismuth-212, complexes with biotin-linked-DOTA conjugates, biological studies 14913-89-4D, complexes with biotin-linked-DOTA conjugates, biological studies 14914-68-2D, Antimony-119, complexes with biotin-linked-DOTA conjugates, biological studies 14967-68-1D, Palladium-103, complexes with biotin-linked-DOTA conjugates, biological studies 14981-64-7D, Palladium-109, complexes with biotin-linked-DOTA conjugates, biological studies 14981-79-4D, Praseodymium-143, complexes with biotin-linked-DOTA conjugates, biological studies 14998-63-1D, Rhenium-186, complexes with biotin-linked-DOTA conjugates, biological studies 15092-94-1D, Lead-212, complexes with biotin-linked-DOTA conjugates, biological studies 15735-74-7D, Platinum-197, complexes with biotin-linked-DOTA conjugates, biological studies 15750-15-9D, Indium-111, complexes with biotin-linked-DOTA conjugates, biological studies 15756-62-4D, Ruthenium-95, complexes with biotin-linked-DOTA conjugates, biological studies 15757-14-9D, Gallium-68, complexes with biotin-linked-DOTA conjugates, biological studies 15757-86-5D, Copper-67, complexes with biotin-linked-DOTA conjugates, biological studies 15758-35-7D, Ruthenium-97, complexes with biotin-linked-DOTA conjugates, biological studies 15760-04-0D, Silver-111, complexes with biotin-linked-DOTA conjugates, biological studies 15765-78-3D, Rhenium-189, complexes with biotin-linked-DOTA conjugates, biological studies 15766-00-4D, Samarium-153, complexes with biotin-linked-DOTA conjugates, biological studies 60239-18-1D, DOTA, biotin-linker conjugates, metal complexes 60239-18-1D, DOTA, biotin-D-amino acid linked 177959-15-8D, linker between biotin and DOTA 227948-63-2D, linker between biotin and DOTA 227948-64-3D, linker between biotin and DOTA 227948-65-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)

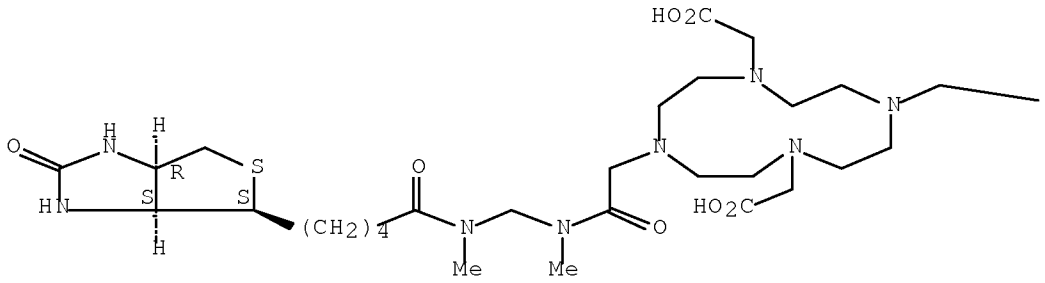
IT 227948-65-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)

RN 227948-65-4 ZCAPLUS

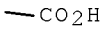
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]methylamino]methyl]methylamino]-2-oxoethyl]- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L80 ANSWER 30 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:579696 ZCAPLUS Full-text
DOCUMENT NUMBER: 127:228839
TITLE: Pharmaceutical agents containing perfluoroalkyl-containing metal complexes and the use thereof in tumor therapy and intervention al radiology
INVENTOR(S): Platzek, Johannes; Niedballa, Ulrich; Raduchel, Bernd; Schlecker, Wolfgang; Weinmann, Hanns-Joachim; Frenzel, Thomas
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9730969		A1	19970828	WO 1997-EP684		19970214
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN						
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE						
DE 19608278		A1	19970828	DE 1996-19608278		19960223
CA 2247253		A1	19970828	CA 1997-2247253		19970214
AU 9717692		A	19970910	AU 1997-17692		19970214
EP 882010		A1	19981209	EP 1997-903278		19970214
EP 882010		B1	20010502			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI						
JP 2000504736		T	20000418	JP 1997-529766		19970214
AT 200894		T	20010515	AT 1997-903278		19970214
ES 2158493		T3	20010901	ES 1997-903278		19970214
PT 882010		T	20011030	PT 1997-903278		19970214
US 6180113		B1	20010130	US 1997-801983		19970219
ZA 9701537		A	19971030	ZA 1997-1537		19970221
TW 477699		B	20020301	TW 1997-86102174		19970222
NO 9803875		A	19981022	NO 1998-3875		19980821
NO 323547		B1	20070611			
GR 3036306		T3	20011031	GR 2001-401156		20010731
PRIORITY APPLN. INFO.:				DE 1996-19608278	A	19960223
				US 1996-12506P	P	19960229
				WO 1997-EP684	W	19970214

OTHER SOURCE(S): MARPAT 127:228839

AB The invention relates to pharmaceutical agents containing perfluoro alkylated metal complexes RF-L-A and the use thereof in tumor therapy and interventional radiol., in which formula RF is a perfluorinated, straight-chain or branched C chain with the formula -CnF2nX (X = terminal F, Cl, Br, I or H atom and n = 4-30), L is a binding group, and A is a metal complex or the salts thereof of organic and/or inorg. bases or amino acids or amino acid amides. Thus Gd/Dy/Y/Mn complexes of tetraazacyclododecane having amide pendants with perfluoroalkyl groups or polyaminopolycarboxylic acids with pendants containing perfluoroalkyl groups were prepared

IC ICM C07C229-06
ICS C07C229-76; C07C237-12; C07C311-00; C07D257-02; A61K033-00; C07F001-00; C07F003-00; C07F005-00; C07F007-00

CC 78-7 (Inorganic Chemicals and Reactions)
Section cross-reference(s): 8, 23, 28, 63

ST lanthanide polyaminopolycarboxylate tetraazacyclododecane perfluoroalkyl pendant prepn; tetraazacyclododecane perfluoroalkyl pendant lanthanide manganese prepn; gadolinium polyaminopolycarboxylate tetraazacyclododecane perfluoroalkyl pendant prepn; dysprosium polyaminopolycarboxylate tetraazacyclododecane perfluoroalkyl pendant prepn; yttrium polyaminopolycarboxylate tetraazacyclododecane perfluoroalkyl pendant prepn; polyaminopolycarboxylate perfluoroalkyl pendant lanthanide prepn; tumor therapy perfluoroalkyl pendant aza complex; interventional radiol perfluoroalkyl pendant aza complex

IT Antitumor agents
(rare earth and manganese perfluoroalkyl-containing tetraazacyclododecane and polyaminopolycarboxylate complexes)

IT 195047-10-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(for preparation of rare earth/manganese complexes for use as pharmaceutical
agents in tumor therapy and interventional radiol.)

IT 98-59-9, p-Toluenesulfonyl chloride 100-46-9, Benzylamine, reactions

106-89-8, reactions 107-15-3, 1,2-Ethanediamine, reactions 108-30-5, Succinic acid anhydride, reactions 108-55-4, Glutaric acid anhydride 110-85-0, Piperazine, reactions 111-26-2, Hexylamine 111-40-0 112-29-8, n-Decyl bromide 112-60-7, Tetraethylene glycol 123-31-9, 1,4-Benzenediol, reactions 143-33-9, Sodium cyanide 294-90-6, 1,4,7,10-Tetraazacyclododecane 307-35-7, Perfluorooctylsulfonyl fluoride 598-21-0, Bromoacetyl bromide 603-35-0, Triphenylphosphine, reactions 647-42-7, 3,3,4,4,5,5,6,6,7,7,8,8,8-Tridecafluoro-1-octanol 678-39-7, 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-decanol 1138-80-3, Benzyloxycarbonylglycine 1738-76-7, Glycine benzyl ester p-toluenesulfonate 2016-57-1, Decylamine 2043-47-2, 3,3,4,4,5,5,6,6,6-Nonafluoro-1-hexanol 2043-53-0 2043-57-4 2566-20-3, N-Benzyloxycarbonyltriglycine 2834-05-1, 11-Bromoundecanoic acid 4151-50-2 4799-67-1, Glycerin-1-monobenzyl ether 5292-43-3, tert-Butyl bromoacetate 6117-80-2 7148-74-5, 2-Bromopropionyl chloride 23911-26-4, Diethylenetriaminepentaacetic acid dianhydride 25711-25-5, N-Benzyloxycarbonylaziridine 30670-30-5, 1H,1H,2H,2H-Perfluorodecylamine 34143-74-3, 1H,1H,2H,2H-Perfluorodecanethiol 38436-14-5, 1-Bromo-3,3,4,4,5,5,6,6,6-nonafluorohexane 38565-52-5 59524-02-6 78277-26-6, Benzyl 6-bromohexanoate 78277-30-2, Benzyl 11-bromoundecanoate 114873-37-9 121326-92-9 130147-42-1, Pentaerythrite monobenzylether 135984-68-8, 2H,2H-Perfluorodecanal 137679-68-6 146432-43-1 168078-14-6 193530-47-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(for preparation of rare earth/manganese fluoroalkyl-containing polyaminopolycarboxylate/tetraazacyclododecane complexes for use as pharmaceutical agents in tumor therapy and interventional radiol.)

IT 473-25-6P 2991-50-6P 13406-91-2P 50598-29-3P 51740-38-6P 55427-54-8P 89932-70-7P 94190-73-5P 94190-74-6P 113584-32-0P 113823-56-6P 114482-33-6P 122193-68-4P 124628-09-7P 137091-62-4P 147011-35-6P 186095-24-9P 186095-25-0P 186095-26-1P 193528-82-4P 193528-87-9P 193528-89-1P 193528-92-6P 193528-94-8P 193528-98-2P 193529-00-9P 193529-02-1P 193529-04-3P 193529-08-7P 193529-11-2P 193529-13-4P 193529-15-6P 193529-23-6P 193529-25-8P 193529-29-2P 193529-33-8P 193529-35-0P 193529-44-1P 193529-58-7P 193529-60-1P 193529-61-2P 193529-62-3P 193529-63-4P 193529-64-5P 193529-65-6P 193529-66-7P 193529-67-8P 193529-68-9P 193529-73-6P 193529-74-7P 193529-75-8P 193529-76-9P 193529-77-0P 193529-78-1P 193529-79-2P 193529-80-5P 193529-81-6P 193529-82-7P 193529-84-9P 193529-88-3P 193529-89-4P 193529-91-8P 193529-93-0P 193529-95-2P 193529-96-3P 193529-98-5P 193530-00-6P 193530-01-7P 193530-02-8P 193530-04-0P 193530-05-1P 193530-06-2P 193530-07-3P 193530-08-4P 193530-09-5P 193530-10-8P 193530-11-9P 193530-12-0P 193530-13-1P 193530-14-2P 193530-24-4P 193530-26-6P 193530-29-9P 193530-31-3P 193530-44-8P 195046-89-0P 195046-92-5P 195046-94-7P 195047-00-8P 195047-01-9P 195047-03-1P 195047-05-3P 195047-12-2P 195047-13-3P 195047-14-4P 195047-15-5P 195047-16-6P 195047-17-7P 195047-18-8P 195047-19-9P 195047-22-4P 195047-23-5P 195047-24-6P 195047-25-7P 195047-37-1P 195047-39-3P 195047-44-0P 195047-45-1P 195047-46-2P 195047-47-3P 195047-48-4P 195047-49-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(for preparation of rare earth/manganese fluoroalkyl-containing polyaminopolycarboxylate/tetraazacyclododecane complexes for use as pharmaceutical agents in tumor therapy and interventional radiol.)

IT 193528-81-3P 195047-04-2P
RL: BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

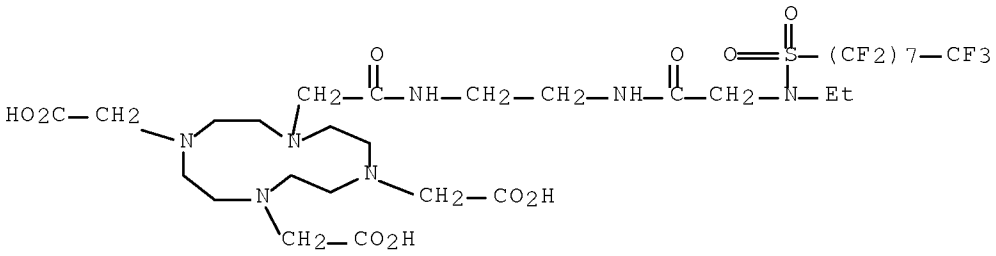
(Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and demetalation and use as pharmaceutical agent in tumor therapy and interventional radiol.)

IT 193528-86-8P 193528-88-0P 193528-90-4P 193528-91-5P
193528-93-7P 193529-09-8P 193529-12-3P 193529-16-7P
193529-24-7P 193529-26-9P 193529-28-1P 193529-30-5P 193529-34-9P
193529-36-1P 193529-41-8P 193529-46-3P 193529-49-6P 193529-52-1P
193529-55-4P 193529-57-6P 193530-48-2P 195046-83-4P 195046-84-5P
195046-86-7P 195046-88-9P 195046-95-8P 195046-98-1P 195046-99-2P
195047-02-0P 195047-06-4P 195047-07-5P 195047-08-6P
195047-09-7P 195047-50-8P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and use as pharmaceutical agent in tumor therapy and interventional radiol.)

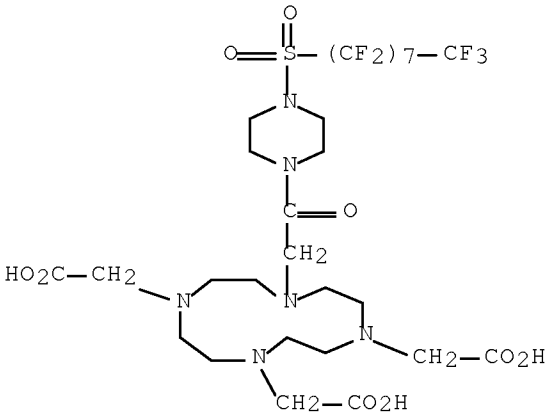
IT 193528-99-3P 193529-01-0P 193529-03-2P 193529-05-4P 195046-90-3P
195046-93-6P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and use as pharmaceutical agent in tumor therapy and interventional radiol..)

IT 193528-92-6P 195047-03-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(for preparation of rare earth/manganese fluoroalkyl-containing polyaminopolycarboxylate/tetraazacyclododecane complexes for use as pharmaceutical agents in tumor therapy and interventional radiol.)

RN 193528-92-6 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(9-ethyl-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluoro-10,10-dioxido-2,7-dioxo-10-thia-3,6,9-triazaoctadec-1-yl)- (CA INDEX NAME)

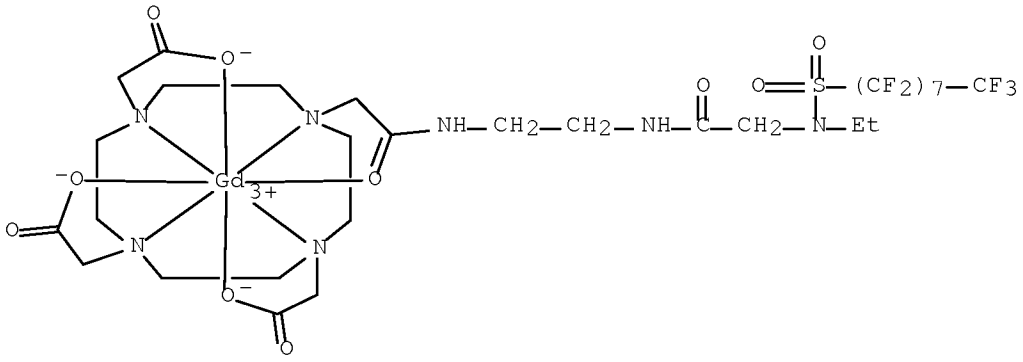


RN 195047-03-1 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[4-[(heptadecafluorooctyl)sulfonyl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

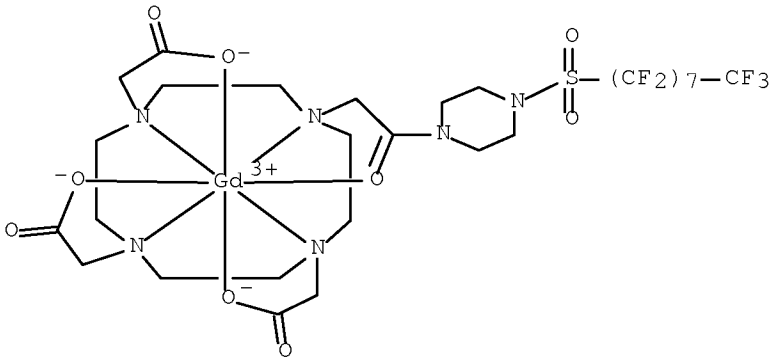


IT 193528-93-7P 195047-02-0P
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and use as pharmaceutical agent in tumor therapy and interventional radiol.)

RN 193528-93-7 ZCAPLUS
CN Gadolinium, [10-[9-ethyl-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluoro-10,10-dioxido-2-(oxo-κO)-7-oxo-10-thia-3,6,9-triazaoctadec-1-yl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-
(9CI) (CA INDEX NAME)



RN 195047-02-0 ZCAPLUS
CN Gadolinium, [10-[2-[4-[(heptadecafluorooctyl)sulfonyl]-1-piperazinyl]-2-(oxo-κO)ethyl]-1,4,7,10-tetraazacyclododecane-1,4,7-triacetato(3-)-κN1,κN4,κN7,κN10,κO1,κO4,κO7]-
(9CI) (CA INDEX NAME)



L80 ANSWER 31 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:184679 ZCAPLUS Full-text
DOCUMENT NUMBER: 126:171905
TITLE: Somatostatin peptides
INVENTOR(S): Albert, Rainer; Bauer, Wilfried; Bruns, Christian; Chandramouli, Nagarajan; Lewis, Ian; Weckbecker, Gisbert
PATENT ASSIGNEE(S): Sandoz Ltd., Switz.; Sandoz-Patent-Gmbh; Sandoz-Erfindungen Verwaltungsgesellschaft M.B.H.; Albert, Rainer; Bauer, Wilfried; Bruns, Christian; Chandramouli, Nagarajan; Lewis, Ian; Weckbecker, Gisbert
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9701579	A2	19970116	WO 1996-EP2840	19960628
WO 9701579	A3	19970227		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
IN 1996MA01094	A	20050304	IN 1996-MA1094	19960620
CA 2222524	A1	19970116	CA 1996-2222524	19960628
AU 9665150	A	19970130	AU 1996-65150	19960628
AU 714447	B2	20000106		
ZA 9605538	A	19971229	ZA 1996-5538	19960628
EP 835263	A2	19980415	EP 1996-924811	19960628
EP 835263	B1	20011205		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI				
CN 1189166	A	19980729	CN 1996-195120	19960628
BR 9609335	A	19990525	BR 1996-9335	19960628
JP 11506108	T	19990602	JP 1996-536834	19960628
JP 3445796	B2	20030908		

HU 9901455	A2	19990928	HU 1999-1455		19960628
HU 9901455	A3	20001128			
RU 2160741	C2	20001220	RU 1998-101506		19960628
AT 210152	T	20011215	AT 1996-924811		19960628
PT 835263	T	20020429	PT 1996-924811		19960628
ES 2169251	T3	20020701	ES 1996-924811		19960628
PL 184947	B1	20030131	PL 1996-323943		19960628
JP 2003104998	A	20030409	JP 2002-208012		19960628
SK 284087	B6	20040908	SK 1997-1770		19960628
IL 122243	A	20050925	IL 1996-122243		19960628
CZ 297381	B6	20061115	CZ 1997-4196		19960628
TW 491854	B	20020621	TW 1996-85109489		19960806
NO 9706064	A	19980216	NO 1997-6064		19971223
NO 317867	B1	20041227			
US 6225284	B1	20010501	US 1997-981426		19971229
HK 1014964	A1	20050408	HK 1999-100124		19990111
PRIORITY APPLN. INFO.:			GB 1995-13224	A	19950629
			GB 1996-429	A	19960110
			JP 1996-536834	A3	19960628
			WO 1996-EP2840	W	19960628

OTHER SOURCE(S): MARPAT 126:171905

AB Somatostatin analogs comprising the amino acid sequence -(D/L)Trp-Lys-X1-X2- [X1 = NHCH(CHMeOCH2R1)CO (R1 = optionally substituted phenyl) or NHCH(CH2R2)CO [R2 = ZCH2R1 (X = O, S), CH2CO2CH2R1, C6H4OCH2R1-p, C6H3(CH2R1)OH-3,4]; X2 is an α-amino acid having an aromatic residue on the Cα side chain or an amino acid unit selected from Dab, Dpr, Dpm, His, (Bzl)HyPro, thienyl-Ala, cyclohexyl-Ala, and tert-Bu-Ala] or their pharmaceutically acceptable salts or complexes with a detectable element were prepared The Lys residue Lys of the sequence corresponds to the Lys9 residue of native somatostatin-14. Thus, cyclo[HyPro-Phe-DTrp-Lys-Tyr(Bzl)-Phe] (I) was prepared by the solid phase method, starting from Fmoc-Phe-SASRIN Resin. IC50 data for binding of I to somatostatin receptor subtypes are tabulated.

IC ICM C07K014-655
ICS A61K038-31

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

ST somatostatin peptide prepn pharmacol property; receptor binding somatostatin peptide; gastric acid secretion somatostatin peptide; antitumor somatostatin peptide; angiogenesis somatostatin peptide; allograft somatostatin peptide; angioplasty somatostatin peptide

IT Angiogenesis
Antitumor agents
(preparation and pharmacol. properties of somatostatin peptides)

IT 50-99-7, D-Glucose, reactions 141-46-8, Hydroxyacetaldehyde 15186-48-8, 2,3-O-Isopropylidene-D-glyceraldehyde 35661-40-6D, resin-bound 57260-73-8 69645-57-4 122350-59-8 134751-65-8 150629-67-7 187223-07-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and pharmacol. properties of somatostatin peptides)

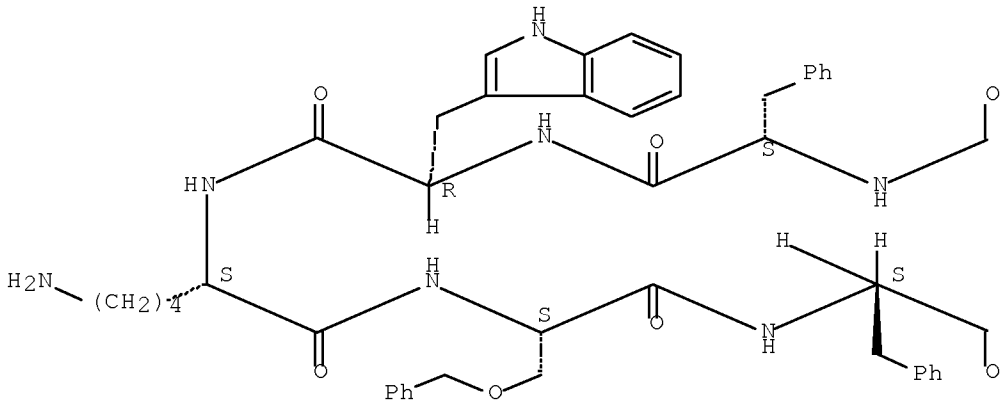
IT 187223-07-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and pharmacol. properties of somatostatin peptides)

RN 187223-07-0 ZCAPLUS

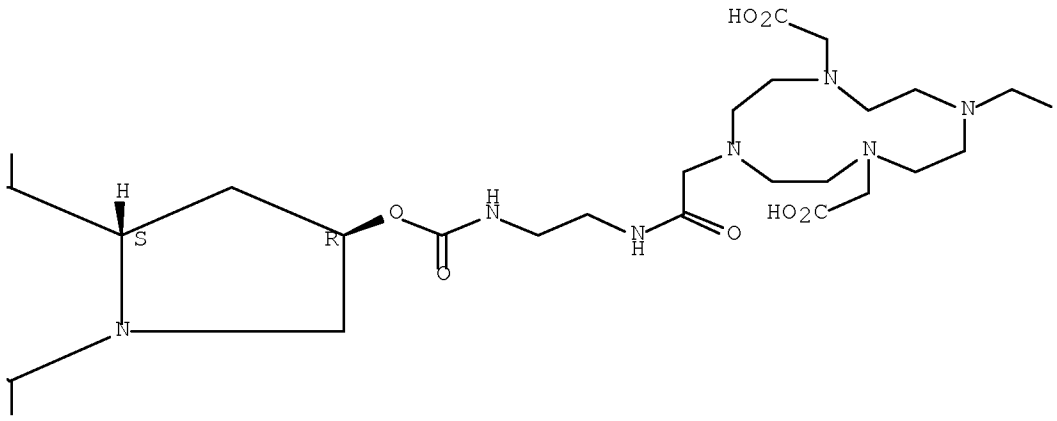
CN Cyclo[L-lysyl-O-(phenylmethyl)-L-seryl-L-phenylalanyl-(4R)-4-[[[[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]carbonyl]oxy]-L-prolyl-L-phenylalanyl-D-tryptophyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 1-C

CO_2H

L80 ANSWER 32 OF 32 ZCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:254285 ZCAPLUS Full-text
DOCUMENT NUMBER: 124:311363
TITLE: Hydrophilic polymer and radioactive metal complexes as

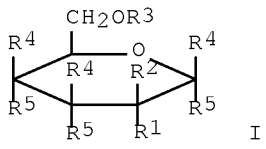
	locally administered radio-therapeutic agents for treatment of cancer and inflammatory diseases
INVENTOR(S):	Seki, Ikuya; Sato, Toku; Seri, Shigemi; Washino, Hiroaki
PATENT ASSIGNEE(S):	Nihon Mediphysics Co Ltd, Japan
SOURCE:	Jpn. Kokai Tokkyo Koho, 19 pp.
	CODEN: JKXXAF
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08012597	A	19960116	JP 1993-290080	19931026
JP 3727074	B2	20051214		

PRIORITY APPLN. INFO.:			JP 1993-290080	19931026

GI



I

AB Biodegradable hydrophilic polymers (polysaccharides and their derivs. containing 1-4 hydrophilic monomer I, with average mol. weight 1 x 103-1 x 106; R1, R2 = H, amino, or hydroxy group; R3 = H, glycol, or carboxymethyl group; R4, R5 = H or hydroxy group) and complex with 1 or >1 radioactive metals are claimed as locally administered radio-therapeutic agents for treatment of cancer and inflammatory diseases. Thus, I were prepared and their pharmacokinetics and antitumor and antiinflammatory effects were studied in mice and rats and discussed with their clin. effectiveness.

IC ICM A61K051-00

CC 8-9 (Radiation Biochemistry)
Section cross-reference(s): 29

ST hydrophilic polymer radioactive metal complex antitumor; antiinflammatory hydrophilic polysaccharide radioactive metal complex

IT 175783-37-6P 175783-38-7P 175892-38-3DP, complex with indium-111 175892-39-4P 175892-40-7P 176199-54-5P
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(hydrophilic polymer and radioactive metal complexes as locally administered radio-therapeutic agents for treatment of cancer and inflammatory diseases)

IT 67-43-6, Diethylenetriamine penta-acetic acid 1398-61-4, Chitin 9012-76-4, Chitosan 10361-82-7, Samarium chloride (SmCl3) 10361-92-9, Yttrium chloride (YCl3) 39271-65-3, Yttrium chloride (90YCl3) 39280-86-9, Glycol chitosan 58259-86-2 149979-17-9, DO 3MA
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrophilic polymer and radioactive metal complexes as locally administered radio-therapeutic agents for treatment of cancer and inflammatory diseases)

IT 175783-40-1P 175783-41-2P 175892-38-3P 175892-42-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(hydrophilic polymer and radioactive metal complexes as locally administered radio-therapeutic agents for treatment of cancer and inflammatory diseases)

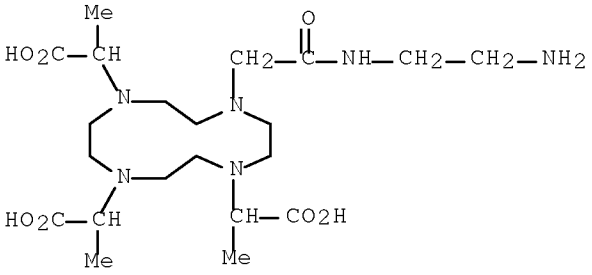
IT 175892-38-3DP, complex with indium-111
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(hydrophilic polymer and radioactive metal complexes as locally administered radio-therapeutic agents for treatment of cancer and inflammatory diseases)

RN 175892-38-3 ZCAPLUS

CN Chitosan, 2-hydroxyethyl ether, polymer with 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-α,α',α''-trimethyl-1,4,7,10-tetraazacyclododecane-1,4,7-tricarboxylic acid (9CI) (CA INDEX NAME)

CM 1

CRN 149979-17-9
CMF C21 H40 N6 O7



CM 2

CRN 39280-86-9
CMF C2 H6 O2 . x Unspecified

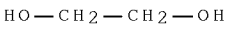
CM 3

CRN 9012-76-4
CMF Unspecified
CCI PMS, MAN

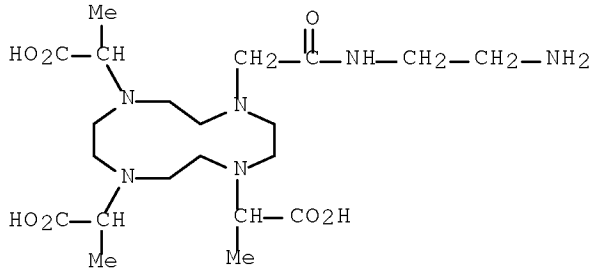
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

CRN 107-21-1
CMF C2 H6 O2



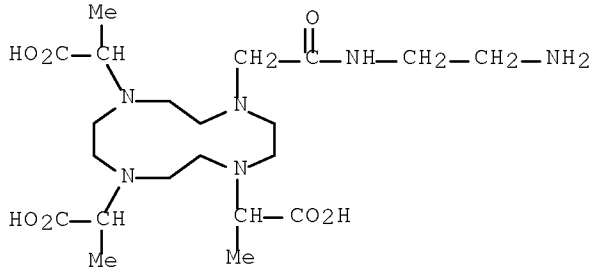
IT 149979-17-9, DO 3MA
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrophilic polymer and radioactive metal complexes as locally administered radio-therapeutic agents for treatment of cancer and inflammatory diseases)
RN 149979-17-9 ZCAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-tricarboxylic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-α,α',α''-trimethyl- (9CI) (CA INDEX NAME)



IT 175892-38-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(hydrophilic polymer and radioactive metal complexes as locally administered radio-therapeutic agents for treatment of cancer and inflammatory diseases)
RN 175892-38-3 ZCAPLUS
CN Chitosan, 2-hydroxyethyl ether, polymer with 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]-α,α',α''-trimethyl-1,4,7,10-tetraazacyclododecane-1,4,7-tricarboxylic acid (9CI) (CA INDEX NAME)

CM 1

CRN 149979-17-9
CMF C21 H40 N6 O7



CM 2

CRN 39280-86-9
CMF C2 H6 O2 . x Unspecified

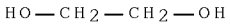
CM 3

CRN 9012-76-4
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 4

CRN 107-21-1
CMF C2 H6 O2



```
=>  d his full

     (FILE 'HOME' ENTERED AT 08:46:48 ON 21 FEB 2008)

     FILE 'ZCAPLUS' ENTERED AT 08:47:31 ON 21 FEB 2008
                E US2006-573938/APPS
L1            1 SEA ABB=ON  PLU=ON  US2006-573938/AP
                D SCA
                SEL RN

     FILE 'REGISTRY' ENTERED AT 08:53:08 ON 21 FEB 2008
L2           65 SEA ABB=ON  PLU=ON  (118726-52-6/BI OR 17137-11-0/BI OR
                294-90-6/BI OR 507475-91-4/BI OR 5292-43-3/BI OR 7429-91-6/BI
                OR 7439-91-0/BI OR 7439-94-3/BI OR 7440-00-8/BI OR 7440-10-0/BI
                 OR 7440-12-2/BI OR 7440-19-9/BI OR 7440-20-2/BI OR 7440-27-9/B
                I OR 7440-30-4/BI OR 7440-45-1/BI OR 7440-52-0/BI OR 7440-53-1/
                BI OR 7440-54-2/BI OR 7440-60-0/BI OR 7440-64-4/BI OR 7440-65-5
                /BI OR 849610-60-2/BI OR 849610-61-3/BI OR 849610-62-4/BI OR
                849610-63-5/BI OR 849610-64-6/BI OR 849610-65-7/BI OR 849610-66
                -8/BI OR 849610-67-9/BI OR 849610-68-0/BI OR 849610-69-1/BI OR
                849610-70-4/BI OR 849610-71-5/BI OR 849610-72-6/BI OR 849610-73
                -7/BI OR 849610-74-8/BI OR 849610-75-9/BI OR 849610-76-0/BI OR
                849610-77-1/BI OR 849610-78-2/BI OR 849610-79-3/BI OR 849610-80
                -6/BI OR 849610-81-7/BI OR 849610-82-8/BI OR 849610-83-9/BI OR
                849610-84-0/BI OR 849610-85-1/BI OR 849610-86-2/BI OR 849610-87
                -3/BI OR 849610-88-4/BI OR 849610-89-5/BI OR 849610-90-8/BI OR
                849610-91-9/BI OR 849610-92-0/BI OR 849610-93-1/BI OR 849610-94
                -2/BI OR 849610-95-3/BI OR 849610-96-4/BI OR 849610-97-5/BI OR
                849610-98-6/BI OR 849610-99-7/BI OR 849611-00-3/BI OR 849680-88
                -2/BI OR 95196-95-5/BI)
                D SCA
L3            1 SEA ABB=ON  PLU=ON  L2 AND NRRS>3
                D SCA

     FILE 'ZCAPLUS' ENTERED AT 09:01:09 ON 21 FEB 2008
L4            1 SEA ABB=ON  PLU=ON  L3

     FILE 'STNGUIDE' ENTERED AT 09:01:27 ON 21 FEB 2008

     FILE 'ZCAPLUS' ENTERED AT 09:03:31 ON 21 FEB 2008
L5        11144 SEA ABB=ON  PLU=ON  L2 (L)  PREP/RL
L6            1 SEA ABB=ON  PLU=ON  L5 AND L1
                D SCA
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 09:04:56 ON 21 FEB 2008
L7           46 SEA ABB=ON  PLU=ON  (118726-52-6/BI OR 17137-11-0/BI OR
                507475-91-4/BI OR 849610-60-2/BI OR 849610-61-3/BI OR 849610-62
                -4/BI OR 849610-63-5/BI OR 849610-64-6/BI OR 849610-65-7/BI OR
                849610-66-8/BI OR 849610-67-9/BI OR 849610-68-0/BI OR 849610-69
                -1/BI OR 849610-70-4/BI OR 849610-71-5/BI OR 849610-72-6/BI OR
                849610-73-7/BI OR 849610-74-8/BI OR 849610-75-9/BI OR 849610-76
                -0/BI OR 849610-77-1/BI OR 849610-78-2/BI OR 849610-79-3/BI OR
                849610-80-6/BI OR 849610-81-7/BI OR 849610-82-8/BI OR 849610-83
                -9/BI OR 849610-84-0/BI OR 849610-85-1/BI OR 849610-86-2/BI OR
                849610-87-3/BI OR 849610-88-4/BI OR 849610-89-5/BI OR 849610-90
                -8/BI OR 849610-91-9/BI OR 849610-92-0/BI OR 849610-93-1/BI OR
                849610-94-2/BI OR 849610-95-3/BI OR 849610-96-4/BI OR 849610-97
```

```
                -5/BI OR 849610-98-6/BI OR 849610-99-7/BI OR 849611-00-3/BI OR
                849680-88-2/BI OR 95196-95-5/BI)

     FILE 'ZCAPLUS' ENTERED AT 09:05:08 ON 21 FEB 2008
L8           76 SEA ABB=ON  PLU=ON  L7
L9              ANALYZE PLU=ON  L8 1- RN HIT :      46 TERMS
                D

     FILE 'REGISTRY' ENTERED AT 09:05:33 ON 21 FEB 2008
L10           1 SEA ABB=ON  PLU=ON  17137-11-0
                D SCA
L11          45 SEA ABB=ON  PLU=ON  L7 NOT L10

     FILE 'ZCAPLUS' ENTERED AT 09:05:59 ON 21 FEB 2008
L12           6 SEA ABB=ON  PLU=ON  L11
                D SCA

     FILE 'REGISTRY' ENTERED AT 09:06:41 ON 21 FEB 2008
L13           0 SEA ABB=ON  PLU=ON  507475-91-4P
L14           1 SEA ABB=ON  PLU=ON  507475-91-4
                D SCA
L15           0 SEA ABB=ON  PLU=ON  95196-95-5P
L16           1 SEA ABB=ON  PLU=ON  95196-95-5
                D SCA
L17          43 SEA ABB=ON  PLU=ON  L11 NOT (L14 OR L15 OR L16)

     FILE 'ZCAPLUS' ENTERED AT 09:07:26 ON 21 FEB 2008
L18           2 SEA ABB=ON  PLU=ON  L17
                D SCA

     FILE 'REGISTRY' ENTERED AT 09:16:14 ON 21 FEB 2008
L19             STRUCTURE UPLOADED
                D SCA L17
L20             STRUCTURE UPLOADED
L21             STRUCTURE UPLOADED
L22          50 SEA SSS SAM L21
                D SCA
L23             STRUCTURE UPLOADED
L24          17 SEA SSS SAM L23
L25             STRUCTURE UPLOADED
L26          50 SEA SSS SAM L25
L27             STRUCTURE UPLOADED
L28           4 SEA SSS SAM L27
                D SCA
                D STAT QUE L28
                D STAT QUE L26
                D STAT QUE L26
L29        2020 SEA SSS FUL L25
                SAVE TEMP L29 PAG938STR25L/A
L30           4 SEA SUB=L29 SSS SAM L27
L31          62 SEA SUB=L29 SSS FUL L27
                SAVE TEMP L31 PAG938STR27L/A

     FILE 'ZCAPLUS' ENTERED AT 09:46:30 ON 21 FEB 2008
L32           9 SEA ABB=ON  PLU=ON  L31

     FILE 'REGISTRY' ENTERED AT 09:47:04 ON 21 FEB 2008
L33          47 SEA ABB=ON  PLU=ON  L31 NOT L17
L34             STRUCTURE UPLOADED
L35           0 SEA SUB=L29 SSS SAM L34
```

```
L36          12 SEA SUB=L29 SSS FUL L34
                D SCA

     FILE 'ZCAPLUS' ENTERED AT 09:53:57 ON 21 FEB 2008
L37           1 SEA ABB=ON  PLU=ON  L36
L38           9 SEA ABB=ON  PLU=ON  L37 OR L32
L39           1 SEA ABB=ON  PLU=ON  L38 AND L1
                SEL RN L38

     FILE 'REGISTRY' ENTERED AT 09:54:59 ON 21 FEB 2008
L40         273 SEA ABB=ON  PLU=ON  (934183-16-1/BI OR 111119-28-9/BI OR
                137076-54-1/BI OR 14265-75-9/BI OR 15750-15-9/BI OR 15757-14-9/
                BI OR 317809-26-0/BI OR 33507-63-0/BI OR 705283-66-5/BI OR
                901439-51-8/BI OR 901439-89-2/BI OR 901442-07-7/BI OR 901443-47
                -8/BI OR 91037-65-9/BI OR 934183-14-9/BI OR 934183-15-0/BI OR
                934350-78-4/BI OR 934350-82-0/BI OR 934350-86-4/BI OR 934350-87
                -5/BI OR 10098-91-6/BI OR 110880-55-2/BI OR 110880-57-4/BI OR
                111844-19-0/BI OR 112188-16-6/BI OR 115608-61-2/BI OR 118726-52
                -6/BI OR 128009-23-4/BI OR 135702-31-7/BI OR 137184-55-5/BI OR
                137813-35-5/BI OR 13967-64-1/BI OR 13967-65-2/BI OR 13981-25-4/
                BI OR 13981-56-1/BI OR 14119-08-5/BI OR 14119-09-6/BI OR
                14133-76-7/BI OR 141743-95-5/BI OR 14191-64-1/BI OR 14265-85-1/
                BI OR 14687-25-3/BI OR 14809-53-1/BI OR 14834-85-6/BI OR
                14885-78-0/BI OR 148893-10-1/BI OR 14913-49-6/BI OR 14981-79-4/
                BI OR 15065-93-7/BI OR 15757-86-5/BI OR 15765-31-8/BI OR
                15776-20-2/BI OR 161552-03-0/BI OR 17137-11-0/BI OR 174267-75-5
                /BI OR 188982-12-9/BI OR 22541-18-0/BI OR 22541-19-1/BI OR
                267410-13-9/BI OR 29022-11-5/BI OR 294-90-6/BI OR 36849-05-5/BI
                 OR 41444-88-6/BI OR 415706-07-9/BI OR 507475-91-4/BI OR
                5292-43-3/BI OR 585531-74-4/BI OR 6066-82-6/BI OR 623575-85-9/B
                I OR 676544-84-6/BI OR 676544-85-7/BI OR 676553-18-7/BI OR
                676553-19-8/BI OR 7087-68-5/BI OR 713520-27-5/BI OR 728914-72-5
                /BI OR 728914-74-7/BI OR 7429-91-6/BI OR 7439-91-0/BI OR
                7439-94-3/BI OR 7440-00-8/BI OR 7440-10-0/BI OR 7440-12-2/BI
                OR 7440-19-9/BI OR 7440-20-2/BI OR 7440-27-9/BI OR 7440-30-4/BI
                 OR 7440-45-1/BI OR 7440-52-0/BI OR 7440-53-1/BI OR 7440-54-2/B
                I OR 7440-60-0/BI OR 7440-64-4/BI OR 7440-65-5/BI OR 766529-14-
                0/BI OR 766529-15-1/BI OR 766529-16-2/BI OR 766529-18-4/BI OR
                766529-19-5/BI OR 766529-20-8/BI OR 766529-22-0/BI OR 766529-24
                -2/BI OR 766529-25-3/BI OR 76652
L41          65 SEA ABB=ON  PLU=ON  L40 AND L2
L42          75 SEA ABB=ON  PLU=ON  L40 AND M/ELS
L43          57 SEA ABB=ON  PLU=ON  L42 NOT L41
L44          38 SEA ABB=ON  PLU=ON  L43 NOT (L31 OR L36)
                D SCA

     FILE 'ZCAPLUS' ENTERED AT 09:59:32 ON 21 FEB 2008
L45           8 SEA ABB=ON  PLU=ON  (L41 OR L42) AND L38

     FILE 'REGISTRY' ENTERED AT 10:00:17 ON 21 FEB 2008
L46         105 SEA ABB=ON  PLU=ON  L29 AND Y/ELS
L47             STRUCTURE UPLOADED
L48           9 SEA SUB=L29 SSS SAM L47
L49         345 SEA SUB=L29 SSS FUL L47
L50         142 SEA ABB=ON  PLU=ON  L49 AND M/ELS
L51         203 SEA ABB=ON  PLU=ON  L49 NOT L50

     FILE 'REGISTRY' ENTERED AT 10:06:58 ON 21 FEB 2008

     FILE 'ZCAPLUS' ENTERED AT 10:07:02 ON 21 FEB 2008
```

```
L52          86 SEA ABB=ON  PLU=ON  L51
L53             ANALYZE PLU=ON  L52 1- RN HIT :     196 TERMS
                D

     FILE 'REGISTRY' ENTERED AT 10:07:38 ON 21 FEB 2008
L54           9 SEA ABB=ON  PLU=ON  L50 AND Y/ELS
                D SCA

     FILE 'ZCAPLUS' ENTERED AT 10:08:22 ON 21 FEB 2008
L55          10 SEA ABB=ON  PLU=ON  L54

     FILE 'REGISTRY' ENTERED AT 10:08:44 ON 21 FEB 2008
L56         112 SEA ABB=ON  PLU=ON  L50 AND LNTH/PG
                D SCA L2

     FILE 'ZCAPLUS' ENTERED AT 10:11:54 ON 21 FEB 2008
L57          36 SEA ABB=ON  PLU=ON  L56
L58          18 SEA ABB=ON  PLU=ON  L32 OR L37 OR L45 OR L55
L59          50 SEA ABB=ON  PLU=ON  L32 OR L37 OR L45 OR L55 OR L57
L60      641196 SEA ABB=ON  PLU=ON  ?TUMOUR?/BI OR ?TUMOR?/BI
L61          39 SEA ABB=ON  PLU=ON  L52 AND L60
L62       25232 SEA ABB=ON  PLU=ON  ?SCAFFOLD?/BI
L63           2 SEA ABB=ON  PLU=ON  L49 AND L62
                D SCA
L64           2 SEA ABB=ON  PLU=ON  (L51 OR L56) AND L62
L65          40 SEA ABB=ON  PLU=ON  (L51 OR L56) AND L60
L66          50 SEA ABB=ON  PLU=ON  L58 OR L64 OR L65
L67           8 SEA ABB=ON  PLU=ON  (L64 OR L65) AND L58
L68          96 SEA ABB=ON  PLU=ON  GARLICH J?/AU
L69          49 SEA ABB=ON  PLU=ON  SUHR R?/AU
L70         710 SEA ABB=ON  PLU=ON  PATTERSON M?/AU
L71           5 SEA ABB=ON  PLU=ON  L68 AND (L69 OR L70)
L72           4 SEA ABB=ON  PLU=ON  L69 AND L70
L73           5 SEA ABB=ON  PLU=ON  (L71 OR L72)
L74           1 SEA ABB=ON  PLU=ON  L29 AND (L68 OR L69 OR L70)

     FILE 'REGISTRY' ENTERED AT 10:20:26 ON 21 FEB 2008

     FILE 'ZCAPLUS' ENTERED AT 10:20:39 ON 21 FEB 2008
                D STAT QUE L32

     FILE 'REGISTRY' ENTERED AT 10:20:59 ON 21 FEB 2008

     FILE 'ZCAPLUS' ENTERED AT 10:21:01 ON 21 FEB 2008
                D STAT QUE L73
                D STAT QUE L74
L75           5 SEA ABB=ON  PLU=ON  (L73 OR L74)

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 10:21:26 ON 21 FEB 2008
L76           1 SEA ABB=ON  PLU=ON  L73

     FILE 'WPIX' ENTERED AT 10:21:40 ON 21 FEB 2008
L77           2 SEA ABB=ON  PLU=ON  (L71 OR L72)

     FILE 'STNGUIDE' ENTERED AT 10:21:48 ON 21 FEB 2008

     FILE 'ZCAPLUS, EMBASE, WPIX' ENTERED AT 10:22:04 ON 21 FEB 2008
L78           5 DUP REM L75 L76 L77 (3 DUPLICATES REMOVED)
                      ANSWERS '1-5' FROM FILE ZCAPLUS
                D IBIB ABS HITIND HITSTR L78 1-5
```

```
     FILE 'REGISTRY' ENTERED AT 10:22:51 ON 21 FEB 2008

     FILE 'ZCAPLUS' ENTERED AT 10:22:54 ON 21 FEB 2008
                D STAT QUE L32
                D STAT QUE L37
                D STAT QUE L45
                D STAT QUE L55
                D STAT QUE L67
L79           17 SEA ABB=ON  PLU=ON  (L32 OR L37 OR L45 OR L55 OR L67) NOT (L73
                OR L74)
                D IBIB ABS HITIND HITSTR L79 1-17

     FILE 'REGISTRY' ENTERED AT 10:26:43 ON 21 FEB 2008

     FILE 'ZCAPLUS' ENTERED AT 10:26:46 ON 21 FEB 2008
                D STAT QUE L64
                D STAT QUE L65
L80           32 SEA ABB=ON  PLU=ON  (L64 OR L65) NOT  (L79 OR L73 OR L74)
                D IBIB ABS HITIND HITSTR L80 1-32


     FILE HOME

     FILE ZCAPLUS

     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
     for records published or updated in Chemical Abstracts after December
     26, 1996), unless otherwise indicated in the original publications.
     The CA Lexicon is the copyrighted intellectual property of the
     American Chemical Society and is provided to assist you in searching
     databases on STN.  Any dissemination, distribution, copying, or storing
     of this information, without the prior written consent of CAS is
     strictly prohibited.

     FILE COVERS 1907 - 21 Feb 2008  VOL 148 ISS 8
     FILE LAST UPDATED: 20 Feb 2008  (20080220/ED)

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

       This file contains CAS Registry Numbers for easy and accurate
       substance identification.

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   20 FEB 2008  HIGHEST RN 1004854-20-9
     DICTIONARY FILE UPDATES:  20 FEB 2008  HIGHEST RN 1004854-20-9

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

       Please note that search-term pricing does apply when
       conducting SmartSELECT searches.

     REGISTRY includes numerically searchable data for experimental and
     predicted properties as well as tags indicating availability of
```

experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 15, 2008 (20080215/UP).

FILE MEDLINE
FILE LAST UPDATED: 20 Feb 2008 (20080220/UP). FILE COVERS 1949 TO DATE.

MEDLINE has been updated with the National Library of Medicine's revised 2008 MeSH terms. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE
FILE COVERS 1974 TO 20 Feb 2008 (20080220/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

Beginning January 2008, Elsevier will no longer provide EMTREE codes as part of the EMTREE thesaurus in EMBASE. Please update your current-awareness alerts (SDIs) if they contain EMTREE codes.

For further assistance, please contact your local helpdesk.

FILE BIOSIS
FILE COVERS 1926 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 20 February 2008 (20080220/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE WPIX
FILE LAST UPDATED: 20 FEB 2008 <20080220/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200812 <200812/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> IPC Reform backfile reclassification has been loaded to the end of November 2007. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC and 20061231/UPIC, 20070601/UPIC, 20071001/UPIC and 20071130/UPIC. <<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:
http://www.stn-international.com/archive/presentations/DWPIAnaVist2_0710.p

>>> XML document distribution format now available - See HELP XMLDOC <<<

>>> ECLA Codes and Current US National Classifications have been added -
see NEWS and HELP CHANGE <<<

>>> HELP for European Patent Classifications see HELP ECLA, HELP ICO <<<

>>> Updated PDF files in the following links:
http://www.stn-international.de/stndatabases/details/ico_0801.zip
http://www.stn-international.de/stndatabases/details/epc_0801.zip <<<

=>